DECEMBER 2001
VOLUME 46
NUMBER 12
ISSN 0020-1324 RECARE

www.rcjournal.com

RESPIRATORY CARE

A MONTHLY SCIENCE JOURNAL
46TH YEAR—ESTABLISHED 1956

SPECIAL ISSUE

EVIDENCE-BASED MEDICINE IN RESPIRATORY CARE PART II

- Evidence-Based Approach to ARDS
- Evidence-Based Treatments for Acute Asthma
- Evidence-Based Airway Management
- Weaning from Mechanical Ventilation: The Evidence from Clinical Research
- EBM and Sleep Apnea
- The Limits of EBM
- Understanding Why We Agree on the Evidence but Disagree on the Medicine

plus

- ANNUAL INDEXES

Cause.

New for COPD!

And Effective.

Introducing premeasured, premixed DuoNeb.

It's the first and only one-step dual-therapy nebulizer solution for COPD, with improved efficacy over albuterol or ipratropium alone—and no increased safety risk.[1]

DuoNeb is indicated for the treatment of bronchospasm associated with COPD in patients requiring more than one bronchodilator. In a 12-week clinical study, the most common adverse reactions reported with DuoNeb Inhalation Solution were chest pain, pharyngitis, diarrhea, bronchitis, nausea and leg cramps.

Albuterol sulfate can have a significant cardiovascular effect, significant hypokalemia and the potential life-threatening paradoxical bronchospasm. Caution is advised in patients with convulsive disorders, hyperthyroidism, diabetes mellitus, narrow-angle glaucoma, prostatic hypertrophy or bladder-neck obstruction. Co-administration of DuoNeb Inhalation Solution and other sympathomimetic agents may increase the risk of adverse cardiovascular effects.

Please see following page for prescribing information.

DuoNeb™

(ipratropium bromide and albuterol sulfate)

Inhalation Solution

Nebulize 1 QID

The first and only one-step dual-therapy nebulizer solution for COPD.

Vial Contains: 0.5 mg Ipratropium Bromide
3.0 mg Albuterol Sulfate
(equivalent to **2.5 mg** Albuterol Base)

DEY 800-755-5560
www.deyinc.com

© 2001 DEY® 09-773-00 4/01

Circle 119 on product information card

DEY

DuoNeb™

(Ipratropium Bromide 0.5 mg/Albuterol Sulfate 3.0 mg*)

Inhalation Solution

***Equivalent to 2.5 mg albuterol base**

BRIEF SUMMARY OF PRESCRIBING INFORMATION

INDICATIONS AND USAGE

DuoNeb is indicated for the treatment of bronchospasm associated with COPD in patients requiring more than one bronchodilator

CONTRAINDICATIONS

DuoNeb is contraindicated in patients with a history of hypersensitivity to any of its components, or to atropine and its derivatives

WARNINGS

Paradoxical Bronchospasm: In the clinical study of DuoNeb, paradoxical bronchospasm was not observed However, paradoxical bronchospasm has been observed with both inhaled ipratropium bromide and albuterol products and can be life-threatening If this occurs, DuoNeb should be discontinued immediately and alternative therapy instituted

Do Not Exceed Recommended Dose: Fatalities have been reported in association with excessive use of inhaled products containing sympathomimetic amines and with the home use of nebulizers

Cardiovascular Effect: DuoNeb, like other beta adrenergic agonists, can produce a clinically significant cardiovascular effect in some patients as measured by pulse rate, blood pressure, and/or symptoms. Although such effects are uncommon for DuoNeb at recommended doses, if they occur, the drug may need to be discontinued. In addition, beta agonists have been reported to produce ECG changes, such as flattening of the T-wave, prolongation of the QTc interval, and ST segment depression. The clinical significance of these findings is unknown. Therefore, DuoNeb, like other sympathomimetic amines, should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension.

Immediate Hypersensitivity Reactions: Immediate hypersensitivity reactions to albuterol and/or ipratropium bromide may occur after the administration of DuoNeb as demonstrated by rare cases of urticaria, angioedema, rash, pruritus, oropharyngeal edema, bronchospasm, and anaphylaxis

PRECAUTIONS

General

1. Effects Seen with Sympathomimetic Drugs. As with all products containing sympathomimetic amines, DuoNeb should be used with caution in patients with cardiovascular disorders, especially coronary insufficiency, cardiac arrhythmias, and hypertension; in patients with convulsive disorders, hyperthyroidism, or diabetes mellitus; and in patients who are unusually responsive to sympathomimetic amines. Large doses of intravenous albuterol have been reported to aggravate pre-existing diabetes mellitus and ketoacidosis. Additionally, β-agonists may cause a decrease in serum potassium in some patients, possibly through intracellular shunting. The decrease is usually transient, not requiring supplementation

2. Effects Seen with Anticholinergic Drugs. Due to the presence of ipratropium bromide in DuoNeb, it should be used with caution in patients with narrow-angle glaucoma, prostatic hypertrophy, or bladder-neck obstruction.

3. Use in Hepatic or Renal Diseases. DuoNeb has not been studied in patients with hepatic or renal insufficiency It should be used with caution in these patient populations.

Information for Patients

The action of DuoNeb should last up to 5 hours. DuoNeb should not be used more frequently than recommended. Patients should be instructed not to increase the dose or frequency of DuoNeb without consulting their healthcare provider. If symptoms worsen, patients should be instructed to seek medical consultation.

Patients must avoid exposing their eyes to this product as temporary papillary dilation, blurred vision, eye pain, or precipitation or worsening of narrow-angle glaucoma may occur, and therefore proper nebulizer technique should be assured, particularly if a mask is used

If a patient becomes pregnant or begins nursing while on DuoNeb, they should contact their healthcare provider about use of DuoNeb.

See the illustrated Patient's Instruction for Use in the product package insert

Drug Interactions

Anticholinergic agents: Although ipratropium bromide is minimally absorbed into the systemic circulation, there is some potential for an additive interaction with concomitantly used anticholinergic medications. Caution is, therefore, advised in the co-administration of DuoNeb with other drugs having anticholinergic properties.

β-adrenergic agents: Caution is advised in the co-administration of DuoNeb and other sympathomimetic agents due to the increased risk of adverse cardiovascular effects.

β-receptor blocking agents. These agents and albuterol sulfate inhibit the effect of each other. β-receptor blocking agents should be used with caution in patients with hyperreactive airways, and if used, relatively selective β_1 selective agents are recommended

Diuretics: The electrocardiogram (ECG) changes and/or hypokalemia that may result from the administration of non-potassium sparing diuretics (such as loop or thiazide diuretics) can be acutely worsened by β-agonists, especially when the recommended dose of the β-agonist is exceeded. Although the clinical significance of these effects is not known, caution is advised in the co-administration of β-agonist-containing drugs, such as DuoNeb, with non-potassium sparing diuretics.

Monoamine oxidase inhibitors or tricyclic antidepressants: DuoNeb should be administered with extreme caution to patients being treated with monoamine oxidase inhibitors or tricyclic antidepressants, or within 2 weeks of discontinuation of such agents because the action of albuterol sulfate on the cardiovascular system may be potentiated

Carcinogenesis, Mutagenesis, Impairment of Fertility

Albuterol Sulfate: In a 2-year study in Sprague-Dawley rats, albuterol sulfate caused a significant dose-related increase in the incidence of benign leiomyomas of the mesovarium at and above dietary doses of 2 mg/kg (approximately equal to the maximum recommended daily inhalation dose for adults on a mg/m² basis). In another study, this effect was blocked by the coadministration of propranolol, a non-selective beta-adrenergic antagonist.

In an 18-month study in CD-1 mice, albuterol sulfate showed no evidence of tumorigenicity at dietary doses up to 500 mg/kg (approximately 140 times the maximum recommended daily inhalation dose for adults on a mg/m² basis). In a 22-month study in Golden hamsters, albuterol sulfate showed no evidence of tumorigenicity at dietary doses up to 50 mg/kg (approximately 20 times the maximum recommended daily inhalation dose for adults on a mg/m² basis)

Albuterol sulfate was not mutagenic in the Ames test or a mutation test in yeast. Albuterol sulfate was not clastogenic in a human peripheral lymphocyte assay or in an AH1 strain mouse micronucleous assay

Reproduction studies in rats demonstrated no evidence of impaired fertility at oral doses of albuterol sulfate up to 50 mg/kg (approximately 25 times the maximum recommended daily inhalation dose for adults on a mg/m² basis)

Ipratropium bromide. In 2-year studies in Sprague-Dawley rats and CD-1 mice, ipratropium bromide showed no evidence of tumorigenicity at oral doses up to 6 mg/kg (approximately 15 times and 8 times the maximum recommended daily inhalation dose for adults in rats and mice respectively, on a mg/m² basis).

Ipratropium bromide was not mutagenic in the Ames test and mouse dominant lethal test. Ipratropium bromide was not clastogenic in a mouse micronucleous assay

A reproduction study in rats demonstrated decreased conception and increased resorptions when ipratropium bromide was administered orally at a dose of 90 mg/kg (approximately 240 times the maximum recommended daily inhalation dose for adults on a mg/m² basis). These effects were not seen with a dose of 50 mg/kg (approximately 140 times the maximum recommended daily inhalation dose for adults on a mg/m² basis).

Pregnancy

TERATOGENIC EFFECTS: Pregnancy Category C

Albuterol sulfate. *Pregnancy Category C.* Albuterol sulfate has been shown to be teratogenic in mice. A study in CD-1 mice given albuterol sulfate subcutaneously showed cleft palate formation in 5 of 111 (4.5%) fetuses at 0.25 mg/kg (less than the maximum recommended daily inhalation dose for adults on a mg/m² basis) and in 10 of 108 (9.3%) fetuses at 2.5 mg/kg (approximately equal to the maximum recommended daily inhalation dose for adults on a mg/m² basis). The drug did not induce cleft palate formation when administered subcutaneously at a dose of 0.025 mg/kg (less than the maximum recommended daily inhalation dose for adults on a mg/m² basis). Cleft palate formation also occurred in 22 of 72 (30.5%) fetuses from females treated subcutaneously with 2.5 mg/kg isoproterenol (positive control).

A reproduction study in Stride rabbits revealed cranioschisis in 7 of 19 (37%) fetuses when albuterol was administered orally at a dose of 50 mg/kg (approximately 55 times the maximum recommended daily inhalation dose for adults on a mg/m² basis)

A study in which pregnant rats were dosed with radiolabeled albuterol sulfate demonstrated that drug-related material is transferred from the maternal circulation to the fetus

During worldwide marketing experience, various congenital anomalies, including cleft palate and limb defects, have been reported in the offspring of patients being treated with albuterol. Some of the mothers were taking multiple medications during their pregnancies. Because no consistent pattern of defects can be discerned, a relationship between albuterol use and congenital anomalies has not been established.

Ipratropium bromide. *Pregnancy Category B.* Reproduction studies in CD-1 mice, Sprague-Dawley rats and New Zealand rabbits demonstrated no evidence of teratogenicity at oral doses up to 10, 100, and 125 mg/kg respectively (approximately 15, 270, and 680 times the maximum recommended daily inhalation dose for adults on a mg/m² basis). Reproduction studies in rats and rabbits demonstrated no evidence of teratogenicity at inhalation doses up to 1.5 and 1.8 mg/kg respectively (approximately 4 and 10 times the maximum recommended daily inhalation dose for adults on a mg/m² basis). There are no adequate and well-controlled studies of the use of DuoNeb, albuterol sulfate, or ipratropium bromide in pregnant women. DuoNeb should be used during pregnancy only if the potential benefit justifies the potential risk to the fetus.

Labor and Delivery

Oral albuterol sulfate has been shown to delay preterm labor in some reports. Because of the potential of albuterol to interfere with uterine contractility, use of DuoNeb during labor should be restricted to those patients in whom the benefits clearly outweigh the risks.

Nursing Mothers

It is not known whether the components of DuoNeb are excreted in human milk. Although lipid-insoluble quaternary bases pass into breast milk, it is unlikely that ipratropium bromide would reach the infant to an important extent, especially when taken as a nebulized solution. Because of the potential for tumorigenicity shown for albuterol sulfate in some animals, a decision should be made whether to discontinue nursing or discontinue DuoNeb, taking into account the importance of the drug to the mother

Pediatric Use

The safety and effectiveness of DuoNeb in patients below 18 years of age have not been established

Geriatric Use

Of the total number of subjects in clinical studies of DuoNeb, 62 percent were 65 and over, while 19 percent were 75 and over. No overall differences in safety or effectiveness were observed between these subjects and younger subjects, and other reported clinical experience has not identified differences in responses between the elderly and younger patients, but greater sensitivity of some older individuals cannot be ruled out.

ADVERSE REACTIONS

Adverse reaction information concerning DuoNeb was derived from the 12-week controlled clinical trial

ADVERSE EVENTS OCCURRING IN ≥ 1% OF ≥ 1 TREATMENT GROUP(S) AND WHERE THE COMBINATION TREATMENT SHOWED THE HIGHEST PERCENTAGE

Body System COSTART Term	Albuterol n (%)	Ipratropium n (%)	DuoNeb n (%)
NUMBER OF PATIENTS	761	754	765
N (%) Patients with AE	327 (43.0)	329 (43.6)	367 (48.0)
BODY AS A WHOLE			
Pain	8 (1.1)	4 (0.5)	10 (1.3)
Pain chest	11 (1.4)	14 (1.9)	20 (2.6)
DIGESTIVE			
Diarrhea	5 (0.7)	9 (1.2)	14 (1.8)
Dyspepsia	7 (0.9)	8 (1.1)	10 (1.3)
Nausea	7 (0.9)	6 (0.8)	11 (1.4)
MUSCULO-SKELETAL			
Cramps leg	8 (1.1)	6 (0.8)	11 (1.4)
RESPIRATORY			
Bronchitis	11 (1.4)	13 (1.7)	13 (1.7)
Lung Disease	36 (4.7)	34 (4.5)	49 (6.4)
Pharyngitis	27 (3.5)	27 (3.6)	34 (4.4)
Pneumonia	7 (0.9)	8 (1.1)	10 (1.3)
UROGENITAL			
Infection urinary tract	3 (0.4)	9 (1.2)	12 (1.6)

Additional adverse reactions reported in more than 1% of patients treated with DuoNeb included constipation and voice alterations.

In the clinical trial, there was a 0.3% incidence of possible allergic-type reactions, including skin rash, pruritus, and urticaria

Additional information derived from the published literature on the use of albuterol sulfate and ipratropium bromide singly or in combination includes precipitation or worsening of narrow-angle glaucoma, acute eye pain, blurred vision, paradoxical bronchospasm, wheezing, exacerbation of COPD symptoms, drowsiness, aching, flushing, upper respiratory tract infection, palpitations, taste perversion, elevated heart rate, sinusitis, back pain and sore throat.

DOSAGE AND ADMINISTRATION

The recommended dose of DuoNeb is one 3 mL vial administered 4 times per day via nebulization with up to 2 additional 3 mL doses allowed per day, if needed. Safety and efficacy of additional doses or increased frequency of administration of DuoNeb beyond these guidelines has not been studied and the safety and efficacy of extra doses of albuterol sulfate or ipratropium bromide in addition to the recommended doses of DuoNeb have not been studied

The use of DuoNeb can be continued as medically indicated to control recurring bouts of bronchospasm. If a previously effective regimen fails to provide the usual relief, medical advice should be sought immediately, as this is often a sign of worsening COPD, which would require reassessment of therapy

A Pan-LC-Plus™ nebulizer (with face mask or mouthpiece) connected to a PRONE8™ compressor was used to deliver DuoNeb to each patient in one U.S. clinical study. The safety and efficacy of DuoNeb delivered by other nebulizers and compressors have not been established

DuoNeb should be administered via jet nebulizer connected to an air compressor with an adequate air flow equipped with a mouthpiece or suitable face mask

HOW SUPPLIED

DuoNeb is supplied as a 3-mL sterile solution for nebulization in sterile low-density polyethylene unit-dose vials. Cards of five vials are placed into a foil pouch. Supplied in cartons as listed below

NDC 49502-672-30	30 vials per carton
NDC 49502-672-60	60 vials per carton

Store between 2°C and 25°C (36°F and 77°F). Protect from light

DEY

DEY, Napa, CA 94558

03-485-21(BRS) May 2001

1. Gross N, Tashkin D, Miller R, et al. Inhalation by nebulization of albuterol-ipratropium combination (Dey combination) is superior to either agent alone in the treatment of chronic obstructive pulmonary disease. *Respiration.* 1998;65:354-362

Earn Continuing Education Credits TODAY

and Save Time and Money with CRCE Online!

We know how valuable your time can be. With the hectic schedules of today's professionals, finding time for top quality education can be a challenge. But not anymore! CRCE Online offers the most convenient way to obtain your CE credits. CRCE Online provides the best online continuing education by offering:

- **Highest Quality** - Top Industry Presenters
- **Classroom-Type Experience**
- **Flexibility and Convenience**
- **Certificate of Completion**
- **Instant Results**
- **Technical Support** - 24/7
- **Course Options:** Multimedia or Read-and-Learn
- **Simple Registration Process**

For More Information on courses offered or how to register, visit our website **www.aarc.org** or call us at **972-243-2272**.

AMERICAN ASSOCIATION FOR RESPIRATORY CARE
AARC

New! Radical™

signal extraction™ pulse oximeter

breakthrough solutions through radical thinking

radical as a standalone pulse oximeter

radical as a handheld pulse oximeter

radical with SatShare™ as an upgrade to your existing validated monitor[1]

motion and low perfusion study

Oximeter	SpO_2 Sensitivity	SpO_2 Specificity	Drop Out
Masimo SET	99%	97%	0.0%
Agilent Viridia 24 C	78%	90%	1.6%
Agilent CMS Rev B	70%	83%	3.7%
Nellcor N-395	70%	73%	4.0%
Novametrix MARS	40%	42%	2.4%

Barker S.J. Presented at the Society for Technology in Anesthesia Annual Meeting, January 2001.

Now you can standardize on the technology that set the standard.™

Masimo SET®

1-877-4-masimo or www.masimo.com

Instruments and sensors containing Masimo SET technology are identified with the Masimo SET logo. Look for the Masimo SET designation on both the sensors and monitors to ensure accurate pulse oximetry when needed most. Masimo SET®

[1]Contact Masimo for a list of the latest SatShare validated multiparameter monitors which include Datascope, Datex-Ohmeda, GE Medical Systems, Hewlett-Packard/Agilent/Philips, Siemens Medical Systems and Spacelabs Medical.

© 2001 Masimo Corporation. Masimo, SET and ◊ are federally registered trademarks of Masimo Corporation. Radical and SatShare are trademarks of Masimo Corporation. Agilent Viridia, Agilent CMS, Nellcor N-395 and Novametrix MARS are trademarks of their respective entities.

Circle 114 on product information card

CONTENTS

DECEMBER 2001 / VOLUME 46 / NUMBER 12

FOR INFORMATION, CONTACT:

AARC Membership or Other AARC Services
American Association for Respiratory Care
11030 Ables Ln
Dallas TX 75229-4593
(972) 243-2272 • Fax (972) 484-2720
http://www.aarc.org

Therapist Registration or Technician Certification
National Board for Respiratory Care
8310 Nieman Rd
Lenexa KS 66214
(913) 599-4200 • Fax (913) 541-0156
http://www.nbrc.org

Accreditation of Education Programs
Committee on Accreditation for Respiratory Care
1701 W Euless Blvd, Suite 300
Euless TX 76040
(817) 283-2835 • Fax (817) 354-8519
http://www.coarc.com

Grants, Scholarships, Community Projects
American Respiratory Care Foundation
11030 Ables Ln
Dallas TX 75229-4593
(972) 243-2272 • Fax (972) 484-2720

AARC Government Affairs Office
Director of Govt Affairs
Jill Eicher
1225 King St. Second Floor
Alexandria VA 22314
(703) 548-8538 Fax (703) 548-8499
eicher@aarc.org

Director of State Govt Affairs
Cheryl West MHA
8630 Braeswood Pt. #2
Colorado Springs, CO 80920
(719) 535-9970 west@aarc.org

RESPIRATORY CARE

RESPIRATORY CARE (ISSN 0020-1324, USPS 0489-190) is published monthly by Daedalus Enterprises Inc. at 11030 Ables Lane, Dallas TX 75229-4593, for the American Association for Respiratory Care. One volume is published per year beginning each January. Subscription rates are $75 per year in the US, $90 in all other countries (for airmail, add $94).

The contents of the Journal are indexed in *Index Medicus*/MEDLINE, Hospital and Health Administration Index, Cumulative Index to Nursing and Allied Health Literature, EMBASE/Excerpta Medica, and RNdex Library Edition. Abridged versions of RESPIRATORY CARE are also published in Italian, French, and Japanese, with permission from Daedalus Enterprises Inc.

Periodicals postage paid at Dallas TX and at additional mailing offices. POSTMASTER: Send address changes to RESPIRATORY CARE, Membership Office, Daedalus Enterprises Inc, 11030 Ables Lane, Dallas TX 75229-4593.

♾ Printed on acid-free paper
Printed in the United States of America
Copyright © 2001, by Daedalus Enterprises Inc

EVIDENCE-BASED MEDICINE IN RESPIRATORY CARE PART II

A SPECIAL ISSUE

CO-CHAIRS

Shelley C Mishoe PhD RRT FAARC
Dean R Hess PhD RRT FAARC

CONFERENCE PROCEEDINGS

An Evidence-Based Approach to Acute Respiratory Distress Syndrome
by Maureen O Meade—Hamilton, Ontario, Canada and Margaret S Herridge—Toronto, Ontario, Canada **1368**

Evidence-Based Treatments for Acute Asthma
by Brian H Rowe, Marcia L Edmonds, Carol H Spooner—Edmonton, Alberta, Canada and Carlos A Camargo—Boston, Massachusetts **1380**

Evidence-Based Airway Management
by Keith Littlewood and Charles G Durbin Jr—Charlottesville, Virginia **1392**

Weaning from Mechanical Ventilation: The Evidence from Clinical Research
by Maureen O Meade, Gordon H Guyatt, and Deborah J Cook—Hamilton, Ontario, Canada **1408**

Evidence-Based Medicine and Sleep Apnea
by Steven J Heitman and W Ward Flemons—Calgary, Alberta, Canada **1418**

The Limits of Evidence-Based Medicine
by Mark R Tonelli—Seattle, Washington **1435**

Understanding Why We Agree on the Evidence but Disagree on the Medicine
by Gordon D Rubenfeld—Seattle, Washington **1442**

BOOKS, FILMS, TAPES, & SOFTWARE

Users' Guide to the Medical Literature: A Manual for Evidence-Based Clinical Practice (Guyatt G, Rennie D, editors) *and* Users' Guide to the Medical Literature: Essentials of Evidence-Based Clinical Practice (Guyatt G, Rennie D, editors)
reviewed by Henry C Barry—East Lansing, Michigan **1450**

Studying a Study and Testing a Test: How to Read the Medical Evidence, 4th ed (Riegelman RK)
reviewed by Anthony D Slonim—Washington, DC **1451**

Want to get out of the parts business?

GET THE GRAB 'N GO SYSTEM, PRAXAIR'S ALL-IN-ONE PORTABLE MEDICAL OXYGEN UNIT.

Praxair's *Grab 'n Go*™ portable medical oxygen system is an oxygen cylinder with a regulator and a contents gauge already attached. It's a fast, easy and safe way to dispense portable oxygen. With a *Grab 'n Go* oxygen unit, you're ready to go at a moment's notice.

Because the *Grab 'n Go* system has no separate parts, you don't waste time searching for and keeping track of equipment. You don't waste money maintaining and repairing equipment. And you don't hassle with wrenches and keys.

With Praxair's *Grab 'n Go* system you have everything you need. The built-in gauge lets you verify contents at a glance. And the easy-to-use regulator lets you adjust oxygen flow with the turn of a dial. The *Grab 'n Go* system also has a handle that makes it a cinch to carry.

Save time. End frustration. And get out of the parts business.

Want to try Praxair's *Grab 'n Go* oxygen system for free? Get up to 20 *Grab 'n Go* units to use in your facility for up to 3 months. To find out more about our demo program, call **1-800-299-7977 ext. 6961**, or visit **www.praxair.com/healthcare**. And while you're at it, check out our extensive line of respiratory gases, equipment and services.

PRAXAIR

Making our planet more productive

PRAXAIR, the FLOWING AIRSTREAM design, GRAB 'N GO and GRAB 'N GO III are either trademarks or registered trademarks of Praxair Technology, Inc., in the United States and/or other countries.
2001, Praxair Technology, Inc. All rights reserved.
P-8564

Circle 111 on product information card

CONTENTS

CONTINUED

ALSO IN THIS ISSUE

1491 AARC Membership Application

1338 Abstracts from Other Journals

1496 Advertisers Index & Help Lines

1496 Author Index

1485 Call for OPEN FORUM Abstracts

1495 Calendar of Events

1487 Manuscript Preparation Guide

1493 New Products

1494 Notices

Evidence-Based Clinical Practice: Concepts and Approaches (Geyman JP, Deyo RA, Ramsey SD) 1452
reviewed by Patricia A Thomas—Baltimore, Maryland

Where's the Evidence: Debates in Modern Medicine (Silverman WA) 1453
reviewed by Mark R Tonelli—Seattle, Washington

Outcome of the Critically Ill: Medicine, Surgery and Trauma (Vukmir RB) 1454
reviewed by C Mark Bazzell—Rochester, Minnesota

Informatics for Healthcare Professionals (Young KM) 1455
reviewed by Steven B Nelson—Overland Park, Kansas

Respiratory & Pulmonary Medicine: July 2000-June 2001: An Internet Resource Guide (Goldenson DR, editor in chief) 1456
reviewed by Steven B Nelson—Overland Park, Kansas

APPRECIATION OF REVIEWERS

Listing of This Year's Manuscript and OPEN FORUM Abstract Reviewers 1457

ANNUAL INDEXES

Author Index for Volume 46 (2001) 1459

Subject Index for Volume 46 (2001) 1466

RESPIRATORY CARE

A Monthly Science Journal
Established in 1956

The Official Journal of the American Association for Respiratory Care

47th International Respiratory Congress
San Antonio, TX
December 1-4, 2001

NEW AND IMPROVED

The New Mirage® Full Face Mask

Series 2

Take a Fresh Look

The best full face mask on the market couldn't wait for the competition. It had to continue the revolution on its own.

REVOLUTIONARY patented double-layer cushion

REVOLUTIONARY Breath-O-Prene® headgear

REVOLUTIONARY patient comfort

Circle 112 on product information car

ResMed

Innovators in Sleep and Respiratory Medicine

www.resmed.com

800 424 0737

BREATH-O-PRENE

Mir[illegible] is a Trademark of ResMed Inc
Bre[illegible] O Prene is a Trademark of
Ac[illegible] MED Technologies Inc

EDITORIAL OFFICE

600 Ninth Avenue, Suite 702
Seattle WA 98104
(206) 223-0558
Fax (206) 223-0563
www.rcjournal.com

MANAGING EDITOR

Ray Masferrer RRT FAARC

ASSISTANT EDITOR

Katherine Kreilkamp

EDITORIAL ASSISTANT

Linda Barcus

COPY EDITOR

Matthew Mero

PRODUCTION

Kelly Piotrowski

MARKETING

Dale L Griffiths
Director of Marketing

Tim Goldsbury
Director, Advertising Sales

Beth Binkley
Advertising Assistant

PUBLISHER

Sam P Giordano MBA
RRT FAARC

RESPIRATORY CARE

A Monthly Science Journal
Established in 1956

The Official Journal of the
American Association for
Respiratory Care

EDITOR IN CHIEF

David J Pierson MD FAARC
Harborview Medical Center
University of Washington
Seattle, Washington

ASSOCIATE EDITORS

Richard D Branson RRT FAARC
University of Cincinnati
Cincinnati, Ohio

Dean R Hess PhD RRT FAARC
Massachusetts General Hospital
Harvard University
Boston, Massachusetts

James K Stoller MD
The Cleveland Clinic Foundation
Cleveland, Ohio

Charles G Durbin Jr MD FAARC
University of Virginia
Charlottesville, Virginia

Neil R MacIntyre MD FAARC
Duke University
Durham, North Carolina

EDITORIAL BOARD

Alexander B Adams MPH RRT FAARC
Regions Hospital
St Paul, Minnesota

Thomas A Barnes EdD RRT FAARC
Northeastern University
Boston, Massachusetts

Joshua O Benditt MD
University of Washington
Seattle, Washington

Michael J Bishop MD
University of Washington
Seattle, Washington

Lluis L Blanch MD PhD
Hospital de Sabadell
Sabadell, Spain

Bartolome R Celli MD
Tufts University
Boston, Massachusetts

Robert L Chatburn RRT FAARC
University Hospitals of Cleveland
Case Western Reserve University
Cleveland, Ohio

Patrick J Dunne MEd RRT FAARC
Health Care Productions
Fullerton, California

James B Fink MS RRT FAARC
Hines VA Hospital
Loyola University
Chicago, Illinois

John E Heffner MD
Medical University of South Carolina
Charleston, South Carolina

Mark J Heulitt MD FAARC
University of Arkansas
Little Rock, Arkansas

Leonard D Hudson MD
University of Washington
Seattle, Washington

Robert M Kacmarek PhD RRT FAARC
Massachusetts General Hospital
Harvard University
Boston, Massachusetts

Richard H Kallet MS RRT
San Francisco General Hospital
University of California San Francisco
San Francisco, California

E Lucy Kester MBA RRT FAARC
The Cleveland Clinic Foundation
Cleveland, Ohio

Max Kirmse MD
University of Erlangen-Nürnberg
Mohrendorf, Germany

Toshihiko Koga MD
Koga Hospital
Kurume, Japan

Marin H Kollef MD
Washington University
St Louis, Missouri

Constantine A Manthous MD
Bridgeport Hospital
Bridgeport, Connecticut

John J Marini MD
University of Minnesota
St Paul, Minnesota

Shelley C Mishoe PhD RRT FAARC
Medical College of Georgia
Augusta, Georgia

Steven B Nelson MS RRT
Overland Park, Kansas
Mayo Clinic
Rochester, Minnesota

Marcy F Petrini PhD
University of Mississippi
Jackson, Mississippi

Joseph L Rau PhD RRT FAARC
Georgia State University
Atlanta, Georgia

Catherine SH Sassoon MD
University of California Irvine
Long Beach, California

John W Shigeoka MD
Veterans Administration Medical Center
Salt Lake City, Utah

Eric J Stern MD
Harborview Medical Center
University of Washington
Seattle, Washington

Martin J Tobin MD
Loyola University
Chicago, Illinois

Jeffrey J Ward MEd RRT
Mayo Medical School
Rochester, Minnesota

Robert L Wilkins PhD RRT FAARC
Loma Linda University
Loma Linda, California

STATISTICAL CONSULTANT

Gordon D Rubenfeld MD
University of Washington
Seattle, Washington

SECTION EDITORS

Hugh S Mathewson MD
Joseph L Rau PhD RRT FAARC
Drug Capsule

Charles G Irvin PhD
Gregg L Ruppel MEd RRT RPFT FAARC
PFT Corner

Richard D Branson RRT FAARC
Robert S Campbell RRT FAARC
Kittredge's Corner

Jon Nilsestuen PhD RRT FAARC
Ken Hargett RRT
Graphics Corner

Patricia Ann Doorley MS RRT
Charles G Durbin Jr MD FAARC
Test Your Radiologic Skill

Editorials, Commentaries, and Reviews to Note

Cardiovascular Complications of Cocaine Use—Lange RA, Hillis LD. N Engl J Med 2001 Aug 2;345(5):351–358.

Complications and Treatment of Mild Hypothermia—Sessler DI. Anesthesiology 2001 Aug; 95(2):531–543.

"Let Me See if I Have This Right. . .": Words that Help Build Empathy—Coulehan JL, Platt FW, Egener B, Frankel R, Lin CT, Lown B, Salazar WH. Ann Intern Med 2001 Aug 7;135(3): 221–227.

Following Protocol: Weaning Difficult-to-Wean Patients with Chronic Obstructive Pulmonary disease (editorial)—Hill NS. Am J Respir Crit Care Med 2001 Jul 15;164(2):186–187.

A New System for Grading Recommendations in Evidence Based Guidelines—Harbour R, Miller J. BMJ 2001 Aug 11;323(7308):334–336.

Safeguarding Patients In Clinical Trials With High Mortality Rates—Freeman BD, Danner RL, Banks SM, Natanson C. Am J Respir Crit Care Med 2001 Jul 15;164(2):190–192.

Improving Survival in Trauma Patients with Acute Respiratory Distress Syndrome (editorial)—Kaisers U, Busch T. Intensive Care Med 2001 Jul;27(7):1113–1115.

Hypoxic Pulmonary Hypertension in Man: What Minimum Daily Duration of Hypoxaemia Is Required? (editorial)—Weitzenblum E, Chaouat A. Eur Respir J 2001 Aug;18(2):251–253.

Why Indirect Calorimetry in Critically Ill Patients: What Do We Want to Measure? (editorial)—Joosten KF. Intensive Care Med 2001 Jul;27(7):1107–1109.

Thunderstorm Outflows Preceding Epidemics of Asthma During Spring and Summer—Marks GB, Colquhoun JR, Girgis ST, Koski MH, Treloar AB, Hansen P, et al. Thorax 2001;56(6):468–471.

BACKGROUND: A study was undertaken to assess the importance of thunderstorms as a cause of epidemics of asthma exacerbations and to investigate the underlying mechanism. METHODS: A case control study was performed in six towns in south eastern Australia. Epidemic case days (n = 48) and a random sample of control days (n = 191) were identified by reference to the difference between the observed and expected number of emergency department attendances for asthma. The occurrence of thunderstorms, their associated outflows and cold fronts were ascertained, blind to case status, for each of these days. In addition, the relation of hourly pollen counts to automatic weather station data was examined in detail for the period around one severe epidemic of asthma exacerbations. The main outcome measure was the number of epidemics of asthma exacerbations. RESULTS: Thunderstorm outflows were detected on 33% of epidemic days and only 3% of control days (odds ratio 15.0, 95% confidence interval 6.0 to 37.6). The association was strongest in late spring and summer. Detailed examination of one severe epidemic showed that its onset coincided with the arrival of the thunderstorm outflow and a 4–12 fold increase in the ambient concentration of grass pollen grains. CONCLUSIONS: These findings are consistent with the hypothesis that some epidemics of exacerbations of asthma are caused by high concentrations of allergenic particles produced by an outflow of colder air, associated with the downdraught from a thunderstorm, sweeping up pollen grains and particles and then concentrating them in a shallow band of air at ground level. This is a common cause of exacerbations of asthma during the pollen season.

Prevalence of Untreated Asthma in a Population Sample of 6000 Older Adults in Bristol, UK—Dow L, Fowler L, Phelps L, Waters K, Coggon D, Kinmonth AL, Holgate ST. Thorax 2001;56(6):472–476.

BACKGROUND: A study was undertaken to estimate the prevalence of untreated asthma in older adults. METHODS: A cross sectional population based survey of 6000 men and women aged 65 years and over was performed in 21 general practices in north Bristol, south west England. The main outcome measure was untreated asthma as defined by a two stage process comprising a respiratory questionnaire (symptoms suggestive of asthma or doctor diagnosed asthma not receiving respiratory treatment) followed by lung function tests (significant reversibility following bronchodilators or corticosteroids and/or significant within day variability in peak expiratory flow). RESULTS: 4792 of the 6000 participants (80%) completed the respiratory questionnaire and, of those not receiving respiratory treatment, 55 reported a previous doctor diagnosis of asthma and a further 696 had symptoms suggestive of asthma. Lung function testing in 280 of 501 randomly selected individuals from these

is what puts it ahead.

PURITAN BENNETT
840 Ventilator System

Modular Design • Dual Microprocessors
SmartAlert™ Alarms • *DualView*™ Touchscreen
BiLevel™ Feature • Tube Compensation

The *840*™ Ventilator system was designed for the future. We're in the hospitals, talking to customers and clinicians, observing treatments and trends. Invest in the *840* ventilator, and get a breath delivery platform that can be upgraded and enhanced as your clinical needs change.

PURITAN BENNETT
Ventilators

Stay ahead in ventilation technology.
Call your Puritan Bennett Sales Representative, or call 1.800.635.5267.

tyco
Healthcare

PURITAN
BENNETT

© 2001 Nellcor Puritan Bennett Inc. All rights reserved.

Circle 109 on product information card

groups resulted in 38 being defined as having asthma and an estimated population prevalence for untreated asthma of 2.4% (95% CI 1.6% to 3.6%) in men and 1.2% (95% CI 0.7% to 2.1%) in women. Most subjects (84%) with untreated asthma had moderate or severe disease. Untreated asthma was most common in individuals with doctor diagnosed asthma (21%) and those with breathlessness or wheeze (13–20%). CONCLUSION: Untreated asthma in the elderly is a common and important problem. Opportunistic use of appropriate lung function tests in older people with a history of doctor diagnosed asthma or wheeze or breathlessness at rest could identify untreated asthmatics who might benefit from treatment.

A Survey of Nocturnal Hypoxaemia and Health Related Quality of Life in Patients with Cryptogenic Fibrosing Alveolitis—Clark M, Cooper B, Singh S, Cooper M, Carr A, Hubbard R. Thorax 2001;56(6):482–486.

BACKGROUND: A survey of overnight oximetry was conducted to estimate the prevalence of nocturnal hypoxaemia in patients with cryptogenic fibrosing alveolitis and to establish whether nocturnal hypoxaemia is related to quality of life. METHODS: All patients with cryptogenic fibrosing alveolitis attending Nottingham City Hospital were invited to enter the study. Spirometric measurements and capillary blood gas tensions were obtained and overnight oxygen saturation was recorded at home. Quality of life was assessed using the Short Form-36, Chronic Respiratory Questionnaire, Hospital Anxiety Depression Scale, and Epworth Sleepiness Score questionnaires. RESULTS: Sixty seven eligible patients were identified and 50 agreed to enter the study, although two were subsequently excluded because they already used oxygen overnight. In the remaining 48 the mean (SD) overnight oxygen saturation (S_{aO_2}) was 92.5 (4.3)% and the median number of dips greater than 4% per hour was 2.3 (interquartile range 1.5–5.3). Daytime oxygen level predicted mean overnight S_{aO_2} (1.94%/kPa, 95% CI 1.22 to 2.66, $p<0.001$) but percentage predicted forced vital capacity (FVC) did not (0.018%/% predicted FVC, 95% CI -0.04 to 0.08, $p=0.5$). Nocturnal hypoxaemia was associated with decreased energy levels and impaired daytime social and physical functioning, and these effects were independent of FVC. CONCLUSIONS: Nocturnal hypoxaemia is common in patients with cryptogenic fibrosing alveolitis and may have an impact on health related quality of life.

Addition of Leukotriene Antagonists to Therapy in Chronic Persistent Asthma: A Randomised Double-Blind Placebo-Controlled Trial—Robinson DS, Campbell D, Barnes PJ. Lancet 2001 Jun 23;357(9273):2007–2011.

BACKGROUND: Controlled trials suggest that leukotriene receptor antagonists can improve lung function and reduce requirement for oral or inhaled corticosteroids in patients with asthma. We aimed to assess whether montelukast, a leukotriene receptor antagonist, can improve symptoms or lung function in patients with chronic asthma with symptoms already taking corticosteroids. METHODS: We did a double-blind, placebo-controlled, crossover, randomised add-on study in which 100 patients with asthma and symptoms despite treatment with inhaled corticosteroids and additional therapy were given 10 mg montelukast sodium for 14 days in an outpatient clinic setting. Outcome measures were symptoms and peak flow diaries. FINDINGS: 72 patients had diary data for analysis. Compared with placebo, addition of montelukast did not result in any significant change in symptom scores (mean difference between the last 7 days of each treatment period 0.05; 95% CI −0.86 to 1.14), rescue inhaled β_2 agonist use (mean difference in puffs per day 0.41; -0.29 to 0.57), or twice daily peak expiratory flow (PEF) measurements (mean difference in morning PEF 1.18 L/min; -14.29 to 17.14), and mean difference in evening peak flow (-0.50; -17.42 to 12.86). When treatment response was defined as a 15% or greater increase in mean peak flow readings, there were four responders to montelukast and seven responders to placebo. INTERPRETATION: Based on PEF data from our previous studies of a similar patient group we would have expected to detect changes of more than 5%. Used as additional therapy in a hospital outpatient clinic setting, montelukast did not provide such additional benefit in patients with moderate or severe asthma.

Diaphragmatic Shape Change After Lung Volume Reduction Surgery—Quint LE, Bland PH, Walker JM, Kazerooni EA, Martinez FJ, Iannettoni MD, Bookstein FL. J Thorac Imaging 2001 Jul;16(3):149–155.

Diaphragmatic shape in normal patients was significantly different from shape in emphysema patients. Postoperative diaphragmatic shape in patients with good clinical outcome differed from preoperative shape and was similar to shape in normal patients. In patients with poor clinical outcome, surgery appeared to have little effect on diaphragm shape.

The Effect of Imaging Modality on Patient Management in the Evaluation of Pulmonary Thromboembolism—Crawford T, Yoon C, Wolfson K, Beller M, Emerick A, Goldin JG, Aberle DR. J Thorac Imaging 2001 Jul;16(3):163–169.

A retrospective medical record review was performed to study the differences in clinical risk profiles and the relationships between test results versus management for suspected pulmonary thromboembolism (TE) in patients undergoing either radionuclide ventilation perfusion ($\dot{V}/\dot{Q}$) scans or pulmonary computed tomographic angiography (CTA), as the initial test. Data of 138 consecutive $\dot{V}/\dot{Q}$ patients were compared with that of 149 consecutive CTA patients during equivalent 6-month intervals before and after the introduction of CTA. Information on risk factors, signs and symptoms, all diagnostic test results, and the relationships between the test results and ultimate physician management were collected and analyzed. $\dot{V}/\dot{Q}$ results predicted physician management in all patients with high probability scans and 91% with normal to low probability scans. There were 35 patients with indeterminate $\dot{V}/\dot{Q}$ scans–43% of these patients were managed without any other diagnostic test. CTA results predicted management in all patients with positive studies and 99% of patients with negative studies. In contrast to the $\dot{V}/\dot{Q}$ cohort, only seven CTA studies were inconclusive–additional diagnostic tests determined management in all but one case. Compared with $\dot{V}/\dot{Q}$, CTA has fewer indeterminate results, is more directly reflective of management, and reduces the number of patients managed with inconclusive data.

Tuberculous fibrosing Mediastinitis: CT and MRI findings—Atasoy C, Fitoz S, Erguvan B, Akyar S. J Thorac Imaging 2001 Jul;16(3):191–193.

Fibrosing mediastinitis is a rare entity usually caused by granulomatous disease. Most cases develop as a complication of histoplasmosis. Mediastinal involvement caused by tuberculosis most often produces focally enlarged lymph nodes, with diffuse mediastinal involvement a very unusual manifestation of disease. The authors describe a patient with extensive tuberculous fibrosing mediastinitis, in whom fibrotic masses produced compression of airways and vascular structures with resultant parenchymal changes.

Sleep and Daytime Sleepiness in Upper Airway Resistance Syndrome Compared to Obstructive Sleep Apnoea Syndrome—Guilleminault C, Do Kim Y, Chowdhuri S, Horita M, Ohayon M, Kushida C. Eur Respir J 2001 May;17(5):838–847.

This study has investigated differences in the nocturnal sleep and daytime sleepiness among patients with obstructive sleep apnoea syndrome (OSAS), upper airway resistance (UARS), sleep hypopnoea syndrome,

More Drug* to the Right Place ... Your Patient's Lungs

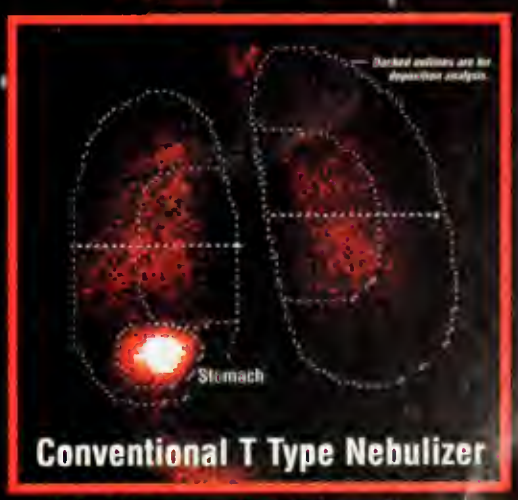
Gamma Camera Deposition Images

AeroEclipse™

Breath Actuated Nebulizer ("BAN")

Dashed outlines are for deposition analysis.

Stomach



Conventional T Type Nebulizer

monaghan™

Monaghan Medical Corporation
P.O. Box 2805 • Plattsburgh, NY 12901-0299
Customer Service 800-833-9653
www.monaghanmed.com

™ trademark ® registered trademark
© 2001 Monaghan Medical Corporation.

Circle 117 on product information card

*Photo Source: *Predicting Lung Deposition with a Cascade Impactor*, Sangwan S., Hull F., Condos R., Smaldone GC. *Journal of Aerosol Medicine* 2001; 14(3):421.

and normal control subjects, using sleep scoring and spectral activity analysis of the electroencephalogram (EEG). Twelve nonobese males with UARS aged 30–60 yrs were recruited. These subjects were strictly matched for age and body mass index with twelve OSAS patients, 12 sleep hypopnoea syndrome patients, and 12 normal controls, all male. Daytime sleepiness was evaluated using the Epworth Sleepiness Scale (ESS) and the Multiple Sleep Latency Test (MSLT). The macrostructure of sleep was determined using international criteria and spectral analysis of the sleep EEG was obtained from a central lead. The sleep macrostructure of OSAS and UARS patients was significantly different from that of controls. These patients were also sleepier during the daytime than controls. Complaints of tiredness and daytime sleepiness, ESS and MSLT scores were similar in the different patient groups. Mild dysmorphia was present in all three patient groups. However, nocturnal sleep was significantly different among the different groups. OSAS patients had significantly more awake time during sleep than the UARS patients. The spectral activity of the total sleep time of the patient groups also differed significantly from that of controls. When the sleep spectral activity of UARS and OSAS patients were compared, OSAS patients had less slow wave sleep activity than UARS patients. UARS patients had a significantly higher absolute power in the 7–9 Hz bandwidth than OSAS patients. The absolute delta power over the different sleep cycles was also different between controls and patients, and between UARS and OSAS patients. There are clear differences in the macrostructure and spectral activity of sleep between upper airway resistance and obstructive sleep apnoea syndrome patients, demonstrated by differences in the cortical activity recorded in the central lead during sleep. Despite these nocturnal sleep differences, the tests of subjective daytime sleepiness are not significantly different.

Outcome of COPD Patients with Mild Daytime Hypoxaemia With or Without Sleep-Related Oxygen Desaturation—Chaouat A, Weitzenblum E, Kessler R, Schott R, Charpentier C, Levi-Valensi P, et al. Eur Respir J 2001 May;17(5):848–855.

The aim of the present study was to compare the evolution of pulmonary haemodynamics and of arterial blood gases in chronic obstructive pulmonary disease (COPD) patients with mild-to-moderate hypoxaemia, with or without sleep-related oxygen desaturation. COPD patients with daytime arterial oxygen partial pressure in the range 56–69 mm Hg were included prospectively. Sleep-related oxygen desaturation was defined as spending $\geq$ 30% of the nocturnal recording time with arterial oxygen saturation $<$ 90%. From the 64 patients included, 35 were desaturators (group 1) and 29 were nondesaturators (group 2). At baseline (t0), patients with sleep-related desaturation had a significantly higher daytime (mean $\pm$ SD) arterial carbon dioxide partial pressure (P_{aCO_2}) (44.9 $\pm$ 4.9 mm Hg versus 41.0 $\pm$ 4.1 mm Hg, $p = 0.001$) whereas mean pulmonary artery pressure (mPAP) was similar in the two groups. After 2 yrs (t2) of follow-up, 22 desaturators and 14 nondesaturators could be re-evaluated, including pulmonary haemodynamic measurements. None of the nondesaturator patients became desaturators at t2. The difference between the two groups in terms of daytime P_{aCO_2} was still present at t2. The mean changes in mPAP from t0 to t2 were similar between the two groups, as were the rates of death or requirement for long-term oxygen therapy (American Thoracic Society criteria) during follow-up of up to 6 yrs. The presence of sleep-related oxygen desaturation is not a transitional state before the worsening of daytime arterial blood gases, but is a characteristic of some chronic obstructive pulmonary disease patients who have a higher daytime arterial carbon dioxide partial pressure. Such isolated nocturnal hypoxaemia or sleep-related worsening of moderate daytime hypoxaemia does not appear to favour the development of pulmonary hypertension, nor to lead to worsening of daytime blood gases.

Factors Associated with Relapse After Ambulatory Treatment of Acute Exacerbations of Chronic Bronchitis. DAFNE Study Group—Miravitlles M, Murio C, Guerrero T. Eur Respir J 2001 May;17(5):928–933.

This study aimed to identify the risk factors for relapse after ambulatory treatment of acute exacerbations of chronic bronchitis (AECB) that can easily be used in a primary care setting. Data were prospectively collected on 2,414 ambulatory patients with AECB from 268 general practices located throughout Spain. A multivariate model to identify risk factors independently associated with failures was developed and validated from the information recorded at the inclusion visit and at 30-days follow-up visit. A total of 507 patients relapsed (21%); of these, 84 required admission (16.5%). The multivariate model for prediction of the risk of relapse included 2,414 cases: 1,689 for the developmental sample and 725 in the validation sample. The model obtained contained three readily-obtainable variables: ischaemic heart disease (odds ratio (OR)=1.63; 95% confidence interval (CI)=1.07–2.47), degree of dyspnoea (OR = 1.31; 1.14–1.50) and number of visits to the general practitioner the previous year (OR = 1.07; 1.04–1.10). The model calibrated well in developmental and validation samples (goodness-of-fit tests: $p = 0.295$ and $p = 0.637$, respectively). Severity of the exacerbation was not associated with increased risk of relapse in either univariate or multivariate analysis. The present results suggest that baseline characteristics of the patients such as degree of dyspnoea, coexisting ischaemic heart disease and number of previous visits to the general practitioner for respiratory problems are strongly associated with increased risk of relapse after ambulatory treatment of acute exacerbations of chronic bronchitis. In contrast, exacerbation severity was not associated with clinical failure. Guidelines for management of acute exacerbations of chronic bronchitis should consider such risk factors and advocate intensive broad spectrum treatment and closer follow-up of patients exhibiting them.

Exhaled Nitric Oxide in Chronic Obstructive Pulmonary Disease: Relationship to Pulmonary Function—Ansarin K, Chatkin JM, Ferreira IM, Gutierrez CA, Zamel N, Chapman KR. Eur Respir J 2001 May;17(5):934–938.

The following study was undertaken in order to determine how exhaled nitric oxide (eNO) levels in former smokers with chronic obstructive pulmonary disease (COPD) compared to eNO levels in patients with asthma and in healthy nonsmoking volunteers. The study also aimed to determine any relationship between eNO levels in COPD and: 1) conventional measures of lung function; and 2) inhaled corticosteroid (ICS) use. In former smokers with COPD, nonsmokers with asthma and volunteers, eNO levels, spirometry, lung volumes, carbon monoxide diffusion capacity of the lung (DL_{CO}) and resting oxygen saturation (S_{aO_2}) were measured. Median eNO was significantly higher among patients with COPD than among healthy volunteers ($p = 0.003$) but lower than among patients with asthma ($p < 0.01$). There was no significant difference in eNO levels between COPD patients using ICS and those not using ICS. By contrast, eNO was lower among asthma patients who used ICS (median 32 parts per billion (ppb); 25–75% range 16–54) than among asthma patients who did not (51 ppb; 32–87) ($p = 0.034$). Among patients with COPD, eNO was inversely correlated with forced expiratory volume in one second, DL_{CO} and S_{aO_2}, and was positively correlated with the residual lung volume/total lung capacity ratio. Among patients with asthma, no significant correlations were found. Exhaled nitric oxide is increased in patients with chronic obstructive pulmonary disease, an increase that is influenced by structural abnormalities of tobacco-induced lung damage.

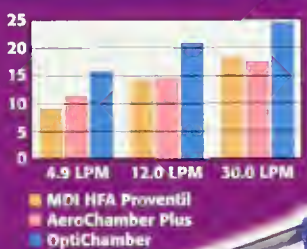
Quality of Life of Idiopathic Pulmonary Fibrosis Patients—De Vries J, Kessels BL, Drent M. Eur Respir J 2001 May;17(5):954–961.

RESPIRONICS®
www.respironics.com

BETTER DESIGN.
BETTER DELIVERY.

OptiChamber® ADVANTAGE

New OptiChamber® Advantage Valved Holding Chamber helps your patients get the best part of their asthma inhaler medication in the most efficient way. With a better design and better delivery, OptiChamber gives you and your patients the advantage in metered dose inhaler therapy.



Better Design

- OptiChamber's new clear mouthpiece and low-resistance valve help parents and caregivers see the valve move, which helps coordinate proper timing of medication actuation.
- Detachable masks allow children to use the holding chamber mouthpiece as soon as possible without the cost of buying a new chamber.
- The valve and end cap are easily removed for cleaning.
- And, OptiChamber's more flexible MDI adapter accommodates a wide variety of CFC and HFA canisters, making it easier to implement a common canister protocol.[1]

Better Delivery

- OptiChamber's optimal larger size (218 mL volume) makes more fine particle dose available for inhalation for patients of all ages.[2,3]

Call 1-800-962-1266 to give your patients the OptiChamber® Advantage today.

1) Wojciechowski W. *Respir Care* 2001;47 (Abstract No. OF-01-122):1082.
2) Data accepted for presentation at the 2001 American College of Allergy, Asthma & Immunology Annual Meeting.
3) Asmus MJ, et al. *Am J Respir Crit Care Med* 2001;163 (5):A444

www.respironics.com

PEOPLE. PRODUCTS. PROGRAMS.

SLEEP MANAGEMENT PROGRAM℠ | CHRONIC RESPIRATORY MANAGEMENT PROGRAM℠ | RESPIRATORY INSUFFICIENCY & FAILURE MANAGEMENT PROGRAM℠ | ASTHMA, ALLERGY & SINUSITIS MANAGEMENT PROGRAM℠ | INFANT MANAGEMENT PROGRAM℠

Respironics HealthScan Asthma & Allergy Products: New Jersey USA • 973-857-3414 • Customer Service: 1-800-962-1266
Global Headquarters: Pittsburgh, Pennsylvania USA • 412-731-2100 • Respironics Europe: +33-(0)1-55-60-19-80 • Respironics Asia Pacific: +852-234-342-18

Circle 103 on product information card

OC0101

Little attention has been paid to quality of life (QOL) in idiopathic pulmonary fibrosis (IPF). Therefore, the aim of this study was to address this issue and study the relationship between QOL, depressive symptoms, and breathlessness in these patients. Forty-one IPF patients and 41 healthy persons matched for age and sex completed the World Health Organization Quality of Life assessment instrument-100. The IPF patients also completed the Beck Depression Inventory, the Bath Breathlessness Scale, a social support questionnaire and a question concerning perceived seriousness of illness. Compared to the control group, QOL in IPF patients was mainly impaired in the domains "physical health" and "level of independence." A number of relationships were found between pulmonary function tests and QOL. The QOL facet "negative feelings" was highly associated with scores on depression. Subjective breathlessness was related to depressive symptoms and QOL. Moreover, sex and effective/emotional breathlessness predicted overall QOL. In conclusion, the impairment of the quality of life areas "physical health" and "level of independence" are important issues in idiopathic pulmonary fibrosis. Subjective breathlessness, especially the effective/emotional scale, seems related to quality of life and depressive symptoms. Rehabilitation programmes are needed that are aimed at physiological aspects and psychosocial aspects of idiopathic pulmonary fibrosis in order to enhance the quality of life of these patients.

Epidemiology of Chronic Obstructive Pulmonary Disease—Anto JM, Vermeire P, Vestbo J, Sunyer J. Eur Respir J 2001 May;17(5):982–994.

Chronic obstructive pulmonary disease (COPD) is a leading cause of world-wide mortality and disability. On average approximately 5–15% of adults in industrialized countries have COPD defined by spirometry. In 1990, COPD was considered to be at the twelfth position world-wide as a cause of combined mortality and disability but is expected to become the fifth cause by the year 2020. COPD has a chronic long-lasting course characterized by irreversible decline of forced expiratory volume in one second (FEV_1), increasing presence of dyspnoea and other respiratory symptoms, and progressive deterioration of health status. After diagnosis the 10-yr survival rate is approximately 50% with more than one-third of patients dying due to respiratory insufficiency. Several environmental exposures such as air pollution increase the risk of death in COPD patients. The aetiology of COPD is overwhelmingly dominated by smoking although many other factors could play a role. Particular genetic variants are likely to increase the susceptibility to environmental factors although little is known about which are the relevant genes. There is clear evidence about the role of the alpha-1-antitrypsin but the fraction of COPD attributable to the relevant variants is only 1%. Phenotypic traits that are considered to play a role in the development of COPD include sex, with females being at a higher risk, bronchial responsiveness and atopy. There is strong causal evidence regarding the relationship between smoking and COPD with decline in FEV_1 levelling off after smoking cessation. Passive smoking has been found to be associated with a small though statistically significant decline in FEV_1. Other risk factors that are likely to be relevant in the development of COPD are occupation, low socioeconomic status, diet and possibly some environmental exposures in early life. Although there is accumulating evidence that oxygen therapy, pharmacological treatment and rehabilitation may improve the course of chronic obstructive pulmonary disease, preventing smoking continues to be the most relevant measure, not only to prevent chronic obstructive pulmonary disease, but also to arrest its development.

Bacteria, Antibiotics and COPD—Wilson R. Eur Respir J 2001 May; 17(5):995–1007.

Bacterial infection is one of several important causes of exacerbations of chronic obstructive pulmonary disease (COPD) that may coexist. COPD is a heterogeneous condition and the incidence of bacterial infection is not uniform; mucus hypersecretion may be an important risk factor. The bacteriology of infections varies depending on the severity of the underlying airway disease. There is now a much better understanding of the pathogenesis of bacterial infections of the respiratory mucosa. Lower airway bacterial colonization may be a stimulus for chronic inflammation and may influence the interval between exacerbations. Antibiotic resistance has increased in all the major pathogens. Antibiotics are an important part of the treatment of acute exacerbations of COPD and the decision about whether to give an antibiotic can be made on clinical grounds. It is more difficult to decide, on the available evidence, whether patient characteristics and the risk of antibiotic resistance should influence choice of empiric antibiotic treatment. Most new antibiotics are modifications of existing structures, suggesting that every effort should be made to conserve the sensitivity of current antibiotics by using them appropriately.

Pulmonary Ventilation Imaged by Magnetic Resonance: At the Doorstep of Clinical Application—Kauczor HU, Chen XJ, van Beek EJ, Schreiber WG. Eur Respir J 2001 May;17(5):1008–1023.

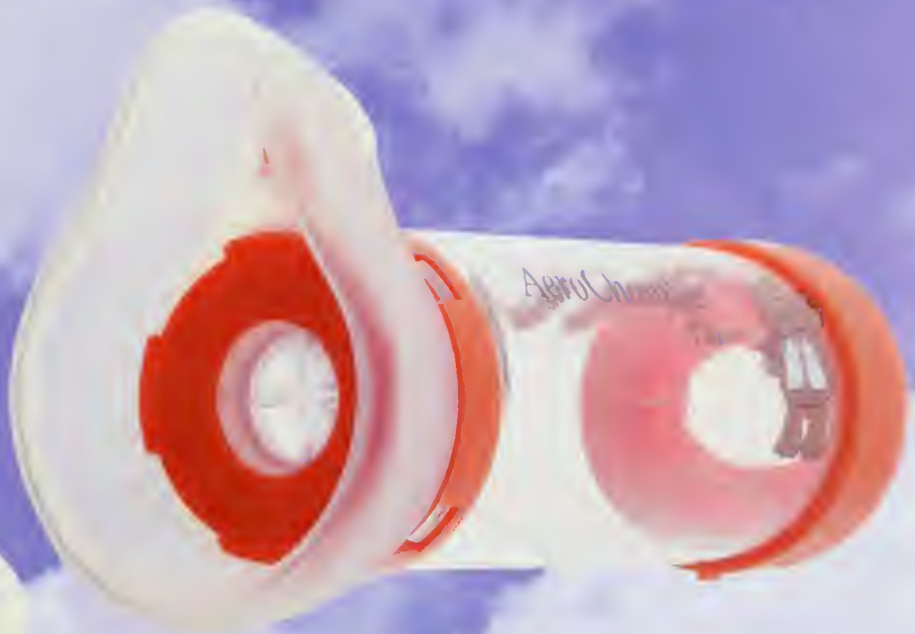
Over the past few years, magnetic resonance imaging (MRI) has emerged as an important instrument for functional ventilation imaging. The aim of this review is to summarize established clinical methods and emerging techniques for research and clinical arenas. Before the advent of MRI, chest radiography and computed tomography (CT) dominated morphological lung imaging, while functional ventilation imaging was accomplished with scintigraphy. Initially, MRI was not used for morphological lung imaging often, due to technical and physical limitations. However, recent developments have considerably improved anatomical MRI, as well as advanced new techniques in functional ventilation imaging, such as inhaled contrast aerosols, oxygen, hyperpolarized noble gases (Helium-3, Xenon-129), and fluorinated gases (sulphur-hexafluoride). Straightforward images demonstrating homogeneity of ventilation and determining ventilated lung volumes can be obtained. Furthermore, new image-derived functional parameters are measurable, such as airspace size, regional oxygen partial pressure, and analysis of ventilation distribution and ventilation/perfusion ratios. There are several advantages to using MRI: lack of radiation, high spatial and temporal resolution and a broad range of functional information. The MRI technique applied in patients with chronic obstructive pulmonary disease, emphysema, cystic fibrosis, asthma, and bronchiolitis obliterans, may yield a higher sensitivity in the detection of ventilation defects than ventilation scintigraphy, CT or standard pulmonary function tests. The next step will be to define the threshold between physiological variation and pathological defects. Using complementary strategies, radiologists will have the tools to characterize the impairment of lung function and to improve specificity.

Urban Air Pollution and Chronic Obstructive Pulmonary Disease: A Review—Sunyer J. Eur Respir J 2001 May;17(5):1024–1033.

There is consistency in the findings that relate the acute increases in urban air pollution (mainly the particulate matter) and the short-term health effects (i.e. mortality and hospital admissions) on patients suffering from chronic obstructive pulmonary disease (COPD). Beyond the acute effects, a relevant public health and scientific question is to what extent chronic exposure to air pollution is related with lung function impairment and development of COPD. The few cross-sectional studies showed an increase of self-reported diagnosis of chronic bronchitis and emphysema, breathlessness and mucus hypersecretion and lower levels of lung function in the more polluted areas. The two cohort studies in children have found a retardation of pulmonary function growth, and the only cohort in adults a faster decline of lung function. Given the intrinsic limitations of cross-sectional studies to separate the timing between exposure and effects, and the weaknesses of the cohorts (ie, few areas, short follow-up, only one retest, lack of individual weighting of air pollution measure) there is a need for new prospective studies. These should be performed in a large number of geographical areas and with a long

Big Relief. *Plus* Performance.

Answering the needs of your smallest patients in big ways.



Alliance of Children's Hospitals, Inc. ACCEPTED

Awarded Seal of Acceptance by The Alliance of Children's Hospitals, Inc.

AARC ZENITH AWARD 1999

REGISTERED ISO 9001 QUALITY SYSTEM

Face Seal Is Critical for Aerosol Delivery.
The ***AeroChamber Plus***™ Valved Holding Chamber ("VHC") with ***ComfortSeal***™ Mask is the only VHC specifically designed for the smaller facial features of a child. *Plus* with its improved design and highly visible exhalation valve, you are assured of a tight mask fit for exceptional performance levels.

Improved Aerosol Suspension Time Delivers Higher Concentrations.
The ***AeroChamber Plus***™ VHC with ***ComfortSeal***™ Mask features a superior rate of drug delivery.* The *Plus*' optimal-sized chamber and Flow Dynamic system can significantly enhance drug delivery at low tidal volumes and low inspiratory flows.

The Only VHC Designed and Built for Children.
From its tamper-resistant valve to the child-friendly *AeroBear*™ instructional graphics, the ***AeroChamber Plus***™ VHC with ***ComfortSeal***™ Mask is designed and built for a child's use. *Plus* it is durable, easy to clean, latex free and offers a new patient and family instructional video and easy-to-read pictorial instructions.

* Compared to competitive devices with many tested drug formulations

FREE VIDEO OFFER
Call 800-833-9653 or email (AeroBear@monaghanmed.com) for a free *AeroBear*™ instructional video cassette. *Limited time offer.*

monaghan™
Monaghan Medical Corporation
PO Box 2805 • Plattsburgh, NY 12901-0299
Customer Service 800-833-9653
www.monaghanmed.com
™ trademarks
©2000 Monaghan Medical Corporation.

Circle 116 on product information card

follow-up to asses the impact of long-term air pollution on lung function growth and decline, and on incidence, duration, severity and survival of chronic obstructive pulmonary disease.

Impact of a Rotating Empiric Antibiotic Schedule on Infectious Mortality in an Intensive Care Unit—Raymond DP, Pelletier SJ, Crabtree TD, Gleason TG, Hamm LL, Pruett TL, Sawyer RG. Crit Care Med 2001 Jun;29(6):1101–1108.

OBJECTIVE: The development of antibiotic-resistant bacteria is associated with significant morbidity and mortality in critically ill patients. We postulated that quarterly rotation of empirical antibiotics could decrease infectious complications from resistant organisms in an intensive care unit (ICU). DESIGN: Prospective cohort study. SETTING: An ICU at a university medical center. SUBJECTS: All patients admitted to the general, transplant, or trauma surgery services who developed pneumonia, peritonitis, or sepsis of unknown origin. INTERVENTIONS: A 2-yr study consisting of 1 yr of nonprotocol-driven antibiotic use and 1 yr of rotating empirical antibiotic assignment. MEASUREMENTS AND MAIN RESULTS: Over 100 variables were recorded for each infectious episode, including patient characteristics (e.g., Acute Physiology and Chronic Health Evaluation [APACHE] II score, age, comorbidities), infection characteristics (e.g., site, organism), treatment characteristics (e.g., antibiotic, treatment duration) and outcome measures (e.g., mortality, length of stay, antibiotic cost). Of 1456 consecutive admissions to the ICU, 540 episodes of infection were treated. No differences were noted in age, APACHE II score, race, overall antibiotic utilization or duration of therapy between the 2 yrs of study. Outcome analysis revealed significant reductions in the incidence of antibiotic-resistant Gram-positive coccal infections (7.8 infections/100 admissions vs. 14.6 infections/100 admissions, $p < .0001$), antibiotic-resistant Gram-negative bacillary infections (2.5 infections/100 admissions vs. 7.7 infections/100 admissions, $p < .0001$), and mortality associated with infection (2.9 deaths/100 admissions vs. 9.6 deaths/100 admissions, $p < 0.0001$) during rotation. Logistic regression identified age (odds ratio [OR], 1.03; 95% confidence interval [CI], 1.01–1.06), APACHE II score (OR, 1.06; 95% CI, 1.01–1.13), solid organ transplantation (OR, 9.50; 95% CI, 2.01–52.21), and malignancy (OR, 10.16; 95% CI, 4.11–26.96) as independent predictors of mortality. Antibiotic rotation was an independent predictor of survival (OR 6.27, 95% CI 2.78–14.16). CONCLUSION: Rotation of empirical antibiotic therapy seems to be a promising method to reduce infectious mortality in an ICU.

Experience with a Clinical Guideline for the Treatment of Ventilator-Associated Pneumonia—Ibrahim EH, Ward S, Sherman G, Schaiff R, Fraser VJ, Kollef MH. Crit Care Med 2001 Jun;29(6):1109–1115.

OBJECTIVE: To evaluate a clinical guideline for the treatment of ventilator-associated pneumonia. DESIGN: Prospective before-and-after study design. SETTING: A medical intensive care unit from a university-affiliated, urban teaching hospital. PATIENTS: Between April 1999 and January 2000, 102 patients were prospectively evaluated. INTERVENTIONS: Prospective patient surveillance, data collection, and implementation of an antimicrobial guideline for the treatment of ventilator-associated pneumonia. MEASUREMENTS AND MAIN RESULTS: The main outcome evaluated was the initial administration of adequate antimicrobial treatment as determined by respiratory tract cultures. Secondary outcomes evaluated included the duration of antimicrobial treatment for ventilator-associated pneumonia, hospital mortality, intensive care unit and hospital lengths of stay, and the occurrence of a second episode of ventilator-associated pneumonia. Fifty consecutive patients with ventilator-associated pneumonia were evaluated in the before period and 52 consecutive patients with ventilator-associated pneumonia were evaluated in the after period. Severity of illness using Acute Physiology and Chronic Health Evaluation II (25.8 ± 5.7 vs. 25.4 ± 8.1, $p = 0.798$) and the clinical pulmonary infection scores (6.6 ± 1.0 vs. 6.9 ± 1.2, $p = 0.105$) were similar for patients during the two treatment periods. The initial administration of adequate antimicrobial treatment was statistically greater during the after period compared with the before period (94.2% vs. 48.0%, $p < 0.001$). The duration of antimicrobial treatment was statistically shorter during the after period compared with the before period (8.6 ± 5.1 days vs. 14.8 ± 8.1 days, $p < 0.001$). A second episode of ventilator-associated pneumonia occurred statistically less often among patients in the after period (7.7% vs. 24.0%, $p = 0.030$). CONCLUSIONS: The application of a clinical guideline for the treatment of ventilator-associated pneumonia can increase the initial administration of adequate antimicrobial treatment and decrease the overall duration of antibiotic treatment. These findings suggest that similar types of guidelines employing local microbiological data can be used to improve overall antibiotic utilization for the treatment of ventilator-associated pneumonia.

Circadian Differences Among 4,096 Emergency Department Patients with Acute Asthma—Brenner BE, Chavda KK, Karakurum MB, Karras DJ, Camargo CA Jr. Crit Care Med 2001 Jun;29(6):1124–1129.

INTRODUCTION: In patients with asthma, airways narrow during the night. The clinical implications of a nocturnal presentation of patients with acute asthma to the emergency department (ED) are uncertain. OBJECTIVE: Our objective was to determine whether patients with asthma who had ED visits during the night (midnight to 7:59 am) vs. other times were more severe, responded less well to ED therapy, and had worse clinical outcomes. DESIGN AND SETTING: We performed a cohort study, as part of the Multicenter Airway Research Collaboration ($n = 77$ sites). ED patients with acute asthma, ages 2–54 yrs, underwent a structured interview in the ED. Chart review of missed/refusal patients created a truly consecutive case series. MEASUREMENTS AND MAIN RESULTS: Among 1,602 children, 19% presented at night. Nighttime patients were more likely to be younger, male, and have a shorter duration of symptoms; there were no other clinical differences noted. Among 2,494 adults, 20% presented at night, and they were more likely to be female and to have a history of steroid use for asthma. Nighttime adults also had a shorter duration of symptoms and slightly lower peak flows (mean, 45% vs. 49% of predicted; $p = 0.006$) and were more likely to receive steroids. They were more likely to be intubated (2.0% vs. 0.2%; $p < 0.001$), but, overall, they were equally likely to be admitted or relapse after ED discharge. In contrast to objective measures of acute asthma severity, both nighttime children and adults were significantly less likely to report their asthma symptoms as severe. CONCLUSION: Except for endotracheal intubation (in adults only), circadian differences minimally affect ED presentation, therapy, or the outcomes of acute asthma. Nighttime asthmatics may be relatively insensitive to the symptoms of severe asthma.

Nitric Oxide Inhalation Increases Alveolar Gas Exchange by Decreasing Deadspace Volume—Skimming JW, Banner MJ, Spalding HK, Jaeger MJ, Burchfield DJ, Davenport PW. Crit Care Med 2001 Jun; 29(6):1195–1200.

OBJECTIVE: To test the hypothesis that nitric oxide inhalation facilitates CO_2 elimination by decreasing alveolar deadspace in an ovine model of acute lung injury. DESIGN: Prospective, placebo-controlled, randomized, crossover model. SETTING: University research laboratory. SUBJECTS: Eleven mixed-breed adult sheep. INTERVENTIONS: To induce acute lung injury, hydrochloric acid was instilled into the tracheas of paralyzed sheep receiving controlled mechanical ventilation. Each sheep breathed 0 ppm, 5 ppm, and 20 ppm nitric oxide in random order. MEASUREMENTS AND MAIN RESULTS: Estimates of alveolar deadspace volumes and arterial-to-end tidal CO_2 partial pressure differences were used as indicators of CO_2 elimination efficiency. At a constant minute

SALTER LABS®

The Tradition Continues for Reliable, Cost Effective Products

DEMAND CANNULA**

Another Innovative, patented design Salter-Style® Cannula. The unmatched standard for long term patient comfort and superior performance with Helios™ or other Dual Port Oxygen Conservation Systems. Available in ADULT, SMALL ADULT and PEDIATRIC sizes...

$O_2Xpress^{®}$

Demand Oxygen Conserver

An all-Pneumatic Oxygen Conserver with a patented design, featuring rapid response and exceptional sensitivity to all patients' varying breathing patterns. Simple, single knob adjustment. Unit delivers a bolus of oxygen in first 1/3 of the inspiratory cycle. $O_2Xpress^{®}$ is proven *clinically equivalent to continuous flow at both rest and exercise*.* Typically extends cylinder duration up to three times.

1.800.235.4203 www.salterlabs.com.

U.S. Patent Nos. *5,666,945, 6,237,015, *5,197,017

* Respiratory Care Oct. 2001, page 1185 (OT-01-193)

Circle 106 on product information card

ventilation, nitric oxide inhalation caused dose-independent decreases in $P_{a(\bar{E})CO_2}$ ($p < 0.05$), alveolar deadspace ($p < 0.01$), and arterial-to-end tidal CO_2 partial pressure differences ($p < 0.01$). We found that estimates of arterial-to-end tidal CO_2 partial pressure differences may be used to predict alveolar deadspace volume ($r^2 = 0.86$, $p < 0.05$). CONCLUSIONS: Estimates of arterial-to-end tidal CO_2 partial pressure differences are reliable indicators of alveolar deadspace. Both values decreased during nitric oxide inhalation in our model of acutely injured lungs. This finding supports the idea that nitric oxide inhalation facilitates CO_2 elimination in acutely injured lungs. Future studies are needed to determine whether nitric oxide therapy can be used to reduce the work of breathing in selected patients with cardiopulmonary disorders.

Effects of the Inspiratory Pressure Waveform During Patient-Triggered Ventilation on Pulmonary Stretch Receptor and Phrenic Nerve Activity in Cats—Ehrhardt H, Sindelar R, Jonzon A, Rieger-Fackeldey E, Schaller P, Schulze A, Sedin G. Crit Care Med 2001 Jun;29(6):1207–1214.

OBJECTIVE: To examine the effects of square wave, sinusoidal, and linear inspiratory pressure waveforms during pressure-controlled assist/control ventilation on the firing pattern of pulmonary stretch receptors and phrenic nerve activity. DESIGN: Experimental, comparative study. SETTING: Research laboratory at a university biomedical center. SUBJECTS: Nine anesthetized, endotracheally intubated young cats (2.5–3.4 kg). INTERVENTION: With interposed periods of continuous positive airway pressure (0.2 kPa), each cat was exposed to periods of assist/control ventilation with three different pressure waveforms, where the peak inspiratory pressure (0.74 ± 0.13 kPa), end-expiratory pressure (0.2 ± 0.02 kPa), and tidal volume (14.9 ± 5.22 mL/kg) were kept constant. Preset controlled ventilator rate was set below the rate of spontaneous breathing, and the mechanical inflation time equaled the inspiratory time during spontaneous breathing on continuous positive airway pressure. MEASUREMENTS AND MAIN RESULTS: Respiratory rate and arterial blood gases did not change between the three pressure waveforms during assist/control ventilation. Peak pulmonary stretch receptor activity was lower and mean phrenic nerve activity higher during continuous positive airway pressure than during assist/control ventilation ($p < 0.05$). Peak inspiratory pulmonary stretch receptor activity was the same with all three pressure waveforms (82 ± 17 impulses · sec^{-1}) but occurred earlier with square wave than with sinusoidal or linear pressure waveforms ($p < 0.05$). The total number of impulses in the phrenic nerve activity burst was smaller with square wave than with the other two pressure waveforms (0.21 ± 0.17 vs. 0.33 ± 0.27 and 0.42 ± 0.30 arbitrary units; $p < 0.05$), and the phrenic nerve activity burst duration was shorter with square wave (1.10 ± 0.45 vs. 1.54 ± 0.36 and 1.64 ± 0.25 secs; $p < 0.05$). CONCLUSION: Square wave pressure waveform during pressure-controlled assist/control ventilation strongly inhibits spontaneous inspiratory activity in cats. One mechanism for this inhibition is earlier and sustained peak pulmonary stretch receptor activity during inspiration. These findings show that differences in inspiratory pressure waveforms influence the spontaneous breathing effort during assist/control ventilation in cats.

Acute Effects of Passive Smoking on the Coronary Circulation in Healthy Young Adults—Otsuka R, Watanabe H, Hirata K, Tokai K, Muro T, Yoshiyama M, et al. JAMA 2001 Jul 25;286(4):436–441.

CONTEXT: Recent studies have shown that passive smoking is a risk factor for ischemic heart disease and may be associated with vascular endothelial dysfunction. The acute effects of passive smoking on coronary circulation in nonsmokers are not known. OBJECTIVE: To determine the acute effects of passive smoking on coronary circulation using coronary flow velocity reserve (CFVR), assessed by noninvasive transthoracic Doppler echocardiography. DESIGN, SETTING, AND PARTICIPANTS: Cross-sectional study conducted from September 2000 to November 2000 among 30 Japanese men (mean age, 27 years; 15 healthy nonsmokers and 15 asymptomatic active smokers) without history of hypertension, diabetes mellitus, or hyperlipidemia. MAIN OUTCOME MEASURES: Coronary flow velocity reserve, calculated as the ratio of hyperemic to basal coronary flow velocity induced by intravenous infusion of adenosine triphosphate and measured in each participant before and after a 30-minute exposure to environmental tobacco smoke. RESULTS: Heart rate and blood pressure responses to adenosine triphosphate infusion were not affected by passive smoking exposure in either group. Passive smoking exposure had no effect on basal coronary flow velocity in either group. Mean (SD) CFVR in nonsmokers was significantly higher than that in active smokers before passive smoking exposure (4.4 [0.91] vs 3.6 [0.88], respectively; $p = 0.02$), while CFVR after passive smoking exposure did not differ between groups ($p = 0.83$). Passive smoking exposure significantly reduced mean (SD) CFVR in nonsmokers (4.4 [0.91] vs 3.4 [0.73], respectively; $p < 0.001$). CONCLUSIONS: Passive smoking substantially reduced CFVR in healthy nonsmokers. This finding provides direct evidence that passive smoking may cause endothelial dysfunction of the coronary circulation in nonsmokers.

The Evolution of β_2-Agonists—Sears MR. Respir Med 2001 Aug;95: S2-S6. β-agonists have been widely used in the treatment of asthma for many years Although concerns have been expressed over their safety based largely upon epidemics of increased mortality in asthmatics associated with high doses of isoprenaline in the 1960s and fenoterol in the 1970s and 1980s, the specific β_2-agonists are vital drugs in asthma management.The short-acting β_2-agonists have an important prophylactic role in the prevention of exercise-induced bronchoconstriction, and are essential in the emergency treatment of severe asthma. However, little if any benefit seems to be derived from regular use of short-acting β_2-agonists and regular or frequent use can increase the severity of the condition. The development of β_2-agonists with long-acting properties, such as salmeterol and formoterol, has provided advantages over short-acting β-agonists, such as prolonged bronchodilation, reduced day- and night-time symptoms and improved quality of sleep, and has reduced the requirement for short-acting β_2-agonists as relief medication. Both drugs are well tolerated and, when added to inhaled corticosteroids, produce greater mprovement in lung function than increased steroid dose alone. Because of its rapid onset of action, formoterol also has the potential to be used for as-needed bronchodilator therapy in asthma.

Pharmacological Similarities and Differences Between β_2-Agonists—Lotvall J. Respir Med 2001 Aug;95:S7-S11.

Formoterol and salmeterol are both long-acting bronchodilators that are effective in the treatment of asthma. However, some differences exist in their pharmacology that are reflected in their clinical profiles. Formoterol has a rapid onset of action, whereas salmeterol causes bronchodilation in a somewhat slower manner. However, both ofthese drugs are long-acting. After single doses clear effects are maintained for 12 h after inhalation, and with high doses effects are observed even at 24 h. Differences between the maximal effects of both drugs are also a consequence of their pharmacological properties. Thus, formoterol has higher intrinsic activity than salmeterol, which means that it is a full agonist, whereas salmeterol is a partial agonist on the β_2-receptor. Physicochemical properties of the drugs may explain the differences in onset and duration of action. Adequate water solubility and moderate lipophilicity of formoterol ensures rapid diffusion to the β_2-receptor on the smooth muscle and rapid bronchodilating activity. Salmeterol, on the other hand, may diffuse more slowly to the β_2-receptor because of its high lipophilicity explaining the slower onset of action. Unlike salbutamol, which is hydrophilic and has a rapid onset and short duration of action, both formoterol and salmeterol possess adequate lipophilic properties to remain in the airway tissues as

a depot in close vicinity to the β_2-receptor, explaining their long duration of effect. The long duration of salmeterol has also been suggested to depend on an anchored binding within the β_2-receptor. The pharmacological evidence for a rapid onset of action of formoterol, but long duration of effect, is supported by several clinical studies. The fast onset of bronchodilation and high intrinsic activity of formoterol therefore suggest that it can be used for relief treatment in patients with asthma if they are concomitantly treated with inhaled glucocorticoids.

Clinical Outcome of Adding Long-Acting β -Agonists to Inhaled Corticosteroids—Barnes PJ. Respir Med 2001 Aug;95:S12-S16.

Current asthma management guidelines state that where a patient is receiving a low to moderate dose of inhaled corticosteroids and is still experiencing symptoms the dose of corticosteroid should be increased and, if necessary, a long-acting bronchodilator should be added. Many studies have now shown that the addition of a β_2-agonist with long-acting properties is more effective at controlling asthma symptoms than increasing the dose of corticosteroid alone. The Formoterol and Corticosteroid Establishing Therapy (FACET) study was a 12-month study comparing exacerbation rates in patients treated with budesonide (100 microg or 400 microg) twice daily alone vs. treatment with budesonide (100 microg or 400 microg) twice daily plus formoterol 9 microg twice daily (delivered dose). The addition of formoterol reduced the rates of mild and severe exacerbations compared with budesonide alone, with the lowest rates seen in patients receiving high-dose budesonide and formoterol. There was no difference in the profile of exacerbations in any groups, indicating formoterol does not mask any signs of inflammation. The addition of formoterol to budesonide was also shown to result in improved lung function (as measured by peak expiratory flow rate and forced expiratory volume in 1 second), night-time awakenings and the use of as-needed medication when compared with an increase in the dose of budesonide. In all cases, increasing the dose of budesonide and addition of formoterol resulted in the most improvement and a significant increase in quality of life, measured by Asthma Quality of Life Questionnaire (AQLQ), was noted. In conclusion, the addition of formoterol to established treatment with inhaled corticosteroids provides superior asthma control compared with an increase in the dose of corticosteroid alone.

The Importance of the Device in Asthma Therapy—Borgstrom L. Respir Med 2001 Aug;95:S26-S29.

Inhalation is the preferred route for drug delivery in asthma treatment. Successful management of asthma depends on achieving adequate delivery of inhaled drug to the lungs, and to this end the role of the device used for delivery is very important. Aerosolized anti-asthma medications have been available for more than 40 years as pressurized metered dose inhalers (pMDIs), but more recently dry powder inhalers (DPIs) have been developed as an alternative. Laboratory assessment of fine particle dose has been shown to correlate to pulmonary deposition if the assessments are performed with an in vivo-like set up. The DPI Turbuhaler delivers a high proportion of the dose as fine particles suggesting high pulmonary deposition. This finding has been confirmed by lung deposition studies, which indicate superior pulmonary deposition from Turbuhaler compared with a pMDI. This superior delivery to the lungs with Turbuhaler is reflected in a better clinical effect, as measured by greater improvements in lung function. The DPIs such as Turbuhaler are easy to use, and Turbuhaler has been shown to function well in a constrained situation such as an acute asthmatic exacerbation. Furthermore, the use of Turbuhaler in acute asthma will provide rapid clinical improvement. The in vivo variability in lung deposition obtained with Turbuhaler is lower than with pMDI, indicating that the performance of Turbuhaler is less dependent on patient competence. Thus, the development of Turbuhaler represents an important step forward in the effective management of asthma.

PREPARE FOR A MAJOR VENTILATOR EMERGENCY

VORTRAN Automatic Resuscitator (VAR)

- Meets FDA and ASTM requirements for a gas-powered, automatic resuscitator
- Cost effective, single patient use
- For breathing and non-breathing patients
- Hands-free operation, fully automatic
- Set up multiple patients at once
- Lightweight, compact size
- Use in and out of the hospital
- Ideal on the scene, in transport and during MRI and CT scans

Call (800) 434-4034 or visit our website at *http://www.vortran.com*

3941 J Street, Suite 354
Sacramento, CA 95819-3633
Tel: (916)648-8460
Fax: (916)648-9751
Website: *www.vortran.com*
E-mail: *office@vortran.com*

Circle 118 on product information card

Flextube Reflectometry for Determination of Sites of Upper Airway Narrowing in Sleeping Obstructive Sleep Apnoea Patients—Faber CE, Hilberg O, Jensen FT, Norregaard O, Grymer L. Respir Med 2001 Aug;95(8):639–648.

The aim of this study was to examine a new technique based on sound reflections in a flexible tube for identifying obstructive sites of the upper airway during sleep. There was no significant difference between two nights in seven obstructive sleep apnoea (OSA) patients regarding the level distribution of pharyngeal narrowings, when the pharynx was divided into two segments (retropalatal and retrolingual). We also compared the level distribution determined by magnetic resonance imaging (MRI) with the level distribution found by flextube reflectometry in seven OSA patients. There was no significant difference between flextube and MRI level distributions during obstructive events, but due to few subjects the power of the test was limited. We found a statistically significant correlation between the number of flextube narrowings per hour of sleep and the number of obstructive apnoeas and hypopnoeas per hour of sleep determined by polysomnography (PSG) in 21 subjects (Spearman's correlation coefficient $r = 0.79$, $p < 0.001$). In conclusion, the flextube reflectometry system seems to be useful for level diagnosis in OSA before and after treatment.

The Clinical Utility of Arterialized Earlobe Capillary Blood in the Assessment of Patients for Long-Term Oxygen Therapy—Eaton T, Rudkin S, Garrett JE. Respir Med 2001 Aug;95(8):655–660.

The prescription of long-term oxygen (LTOT) is underpinned by the measurement of arterial P_{O_2}, generally obtained by radial artery puncture. This test is commonly associated with patient discomfort and a test that is reliable, well-tolerated and non-invasive would be advantageous. Cutaneous oximetry has not proved sufficiently accurate. Arterialized earlobe capillary sampling has been proposed, with some authors stating that it is under-utilized. However, to date studies have yielded conflicting results and the clinical utility remains uncertain. Our regional oxygen service based at a specialist respiratory hospital undertook a prospective study of consecutive patients with chronic respiratory disease undergoing assessment for LTOT. Simultaneous radial artery and arterialized earlobe sampling was performed. Rigorous steps were taken to ensure optimal arterialization of the earlobe samples. Agreement between arterial and arterialized P_{O_2} and P_{CO_2} was compared using the Bland-Altman method. One hundred patients were studied. Procedural difficulties (insufficient sample or air in sample) were similar for both procedures, however clotting occurred more frequently in arterialized earlobe samples. Sixty-four sample pairs were available for comparison. The bias and limits of agreement between arterialized and arterial P_{O_2} were wide, mean (± 2 SD), -048 (-2.05–1.09) kPa.The bias and limits of agreement for P_{CO_2} were smaller. Using the absolute criterion (arterial P_{O_2} <7.3 kPa), 9/55 (16%) patients would receive oxygen inappropriately based on the arterialized earlobe sample. Conversely, no patients would have been denied LTOT. Radial artery puncture gave rise to significantly greater discomfort ($p < 0.0001$) and level of concern ($p < 0.0001$). Patient preference strongly favoured arterialized earlobe sampling. However, despite rigorous attention to arterialization earlobe sampling was insufficiently accurate to replace radial artery puncture in the prescription of LTOT.

Prevalence of Daytime Hypercapnia or Hypoxia in Patients with OSAS and Normal Lung Function—Verin E, Tardif C, Pasquis P. Respir Med 2001 Aug;95(8):693–696.

The purpose of this study was to determine factors increasing daytime P_{aCO_2} or P_{aO_2} in obstructive sleep apnoea syndrome patients (OSAS) with normal pulmonary function tests. Anthropometric, pulmonary function tests, arterial blood gases and sleep polygraphic data were analysed retrospectively in 218 OSAS patients (apnoea-hypopnoea index > 15 h^{-1}; 18 females, 55 ± 11 years): 125 patients had abnormal pulmonary function tests, i.e. one or more flow or volume under 80% or above 120% of predictive value (group I) and 93 had normal pulmonary function tests (group II). Hypercapnia was defined as $P_{aCO_2} \geq 6.0$ kPa and hypoxia as $P_{aO_2} < 9.3$ kPa. Patients with abnormal pulmonary function tests were more hypoxic and hypercapnic, more obese, and had a higher apnoea-hypopnoea index ($p < 0.05$). Seventeen patients of group I and four of group II were hypercapnic (13.6% and 4.3%, respectively). Thirty-one patients in group I (24.8%) had a $P_{aO_2} < 9.3$ kPa and six (6.5%) in group II. Stepwise multiple regression analysis showed that in group II, only two factors were correlated with P_{aCO_2}: mean apnoea duration and FRC (respectively: $c = 0.228$, $p < 0.001$; $c = 0.006$, $p = 0.108$); and only two with P_{aO_2}: mean apnoea duration: ($c = -0.218$, $p = 0.029$) and BMI ($c = -3.72$, $p < 0.0001$). Daytime hypercapnia is present in 4.3% and daytime hypoxia in 6.5% of patients with occlusive sleep apnoea syndrome and normal pulmonary function tests. These alterations in blood gases in OSAS with normal pulmonary function tests should be considered as OSAS severity criteria.

Sleep and Behavior Problems in School-Aged Children—Stein MA, Mendelsohn J, Obermeyer WH, Amromin J, Benca R. Pediatrics 2001 Apr;107(4):E60.

OBJECTIVES: The primary purposes of the present study were to survey the prevalence of sleep problems in school-aged children and to examine these associations with parental perception of sleep problems, medical history, and childhood psychopathology. METHODS: Sleep and medical history questionnaires and the Child Behavior Checklist were administered to the parents of 472 children between ages 4 and 12 years receiving routine pediatric care from urban, rural, and suburban pediatric practices. RESULTS: Although sleep problems were reported for 10.8% of the sample during the past 6 months, less than one half of the parents who identified sleep problems reported that they had discussed sleep with their child's pediatrician. The best predictor of current sleep problems was a history of sleep problems before age 2 years. Sleep problems such as snoring, tiredness during the day, and taking excessive time to fall asleep were very common, occurring at least 1 night per week in over 20% of the total sample. Factor analysis of the sleep problems questionnaire resulted in 5 sleep problem factors that accounted for 58.7% of the variance. Specific sleep problem factors include: parasomnias, enuresis/gags, tiredness, noisy sleep, and insomnia. Sleep problem factor scores were differentially associated with medical history variables and measures of childhood psychopathology. Children rated highly on parasomnias were more likely to have frequent falls and to display pica. Parasomnias and noisy sleep were inversely associated with socioeconomic status (SES). Children from lower SES families were rated higher on these factors than children from higher SES families. Enuresis/gags was the only sleep problem factor associated with age. Younger children scored higher on this factor. Duration of naps was highly correlated with age and with bed times during the week and weekends. As expected, younger children were more likely to nap for longer periods and to have earlier bed times. In addition, higher tiredness factor scores were associated with napping and with later bed times during the week and weekend. Boys were much more likely than were girls to have higher scores on enuresis/gags, and higher enuresis/gags scores were associated with an increased prevalence of trauma and falls. Bed times were not associated with any other sleep problem factor score. Children rated highly on tiredness were more likely to have a history of hospitalizations. Tiredness factor scores were strongly associated with the sleep practice of sharing a bed but not with sharing a room. Sharing a room was not associated with any sleep problem factor score. High scores on noisy sleep were associated with allergies, falls frequently, and with sharing a bed. Children with high scores on the insomnias were also more likely to display an increased prevalence of allergies. CONCLUSIONS: Parental perception of global sleep problems was surprisingly common in school-aged

Cannula Support Band

The solution to the pain and discomfort caused by cannula tubing

- Prevents painful ear sores
- Relieves pressure off the ears
- Replaces all other inadequate devices
- Maintains proper cannula position

Are you or someone you know suffering from the pain and discomfort caused by the use of an oxygen cannula? **The cannula support band** will firmly yet gently hold the cannula in place and off the ears. Machine wash, fully adjustable, feather soft and hypoallergenic. **The cannula support band will bring comfort to an otherwise painful situation.**

$19.95 + 5.50 Postage & Handling
A portion of the proceeds will be donated to the **American Lung Association** with each order.
Large quanity discounts available
Venders welcome

To order call 888-460-8733
or send a check to:
A.B.W. Intl.
P.O. Box 5314
Katy TX. 77491
E-Mail abw@fbcc.com

Circle 120 on product information card

children receiving routine pediatric care. Parental reports of their children's sleep problems may be a red flag for specific sleep problems and psychiatric, social, or medical problems. Sleep problems should be queried about during pediatric visits for school-aged children.

Effectiveness of a High School Smoking Cessation Program—Adelman WP, Duggan AK, Hauptman P, Joffe A. Pediatrics 2001 Apr;107(4): E50.

OBJECTIVE: To evaluate the impact of a school-based smoking cessation program targeting adolescents interested in quitting. DESIGN: Randomized clinical trial over one school year. SETTING: Large public high school. PARTICIPANTS: Students interested in quitting smoking. INTERVENTION: Seventy-four students were randomized to receive either: 1) a 6-week, 8-session, classroom-based, smoking cessation curriculum designed for adolescents (n = 35) or 2) an informational pamphlet on how to quit smoking with promise of the classroom curriculum in 3 months (n = 39). OUTCOME MEASURES: Change in smoking behavior measured by: 1) self-reported smoking cessation and exhaled carbon monoxide <6 parts per million (smoke-free); 2) self-reported quit attempts; and 3) change in cigarettes per day (cpd) at the end of the 6-week curriculum and then 4, 10, and 20 weeks later. Saliva cotinine was also measured at these points to validate these outcome measures. Analysis: Intention-to-treat. RESULTS: Participants in the classroom group attended an average of 4.4 sessions. At the end of the curriculum, the classroom group was significantly more likely to be smoke-free (59% vs 17%), to have tried to quit smoking (82% vs 54%), and to reduce mean cpd (7.0 vs 1.0). Four weeks later, these differences persisted: smoke-free (52% vs 20%), quit attempt (85% vs 60%), and reduction in mean cpd (6.6 vs 1.6). Changes in saliva cotinine were consistent with reported outcome measures: those who were smoke-free had a significant reduction in saliva cotinine at the end of the intervention, and at 4 weeks. At 10 and 20 weeks after the curriculum, 41% and 31%, respectively, of the classroom group remained smoke-free. Once participants in the pamphlet group underwent the classroom intervention (average attendance of 2.2 sessions) their cessation rates were similar to the initial group: 31% at the end of the curriculum and 27% 10 weeks later. CONCLUSION: A school-based curriculum for adolescent smoking cessation is more effective than an informational pamphlet alone and reduces cigarette use by adolescents. More research is needed to test the reproducibility, sustainability, and generalizability of this curriculum to offer more smoking cessation options to teenagers.

Asthma Severity and Adequacy of Management in Accident and Emergency Departments in France: A Prospective Study—Salmeron S, Liard R, Elkharrat D, Muir J, Neukirch F, Ellrodt A. Lancet 2001 Aug 25;358(9282):629–635.

Background: Recent guidelines have enabled doctors to establish accident and emergency department management strategies for acute asthma on the basis of severity of exacerbations at presentation. However, there is no available information on acute asthma patients classified according to severity of disease. Our aim was to describe the severity of such exacerbations at presentation, and the adequacy of treatment and management. Methods: We did a 12-month multicentre cross-sectional observational cohort study in adult patients with acute asthma who attended one of 37 accident and emergency departments in France. The doctors who examined the patients obtained information using a formatted chart. We classified exacerbations according to severity (life-threatening, severe, or mild to moderate), on the basis of clinical findings and peak expiratory flow value, as defined by currently used guidelines. Findings: Of 3772 patients with acute asthma, 975 (26%) had life-threatening attacks, 1834 (49%) had severe exacerbations without life-threatening features, and 963 (26%) had mild to moderate exacerbations. Initial treat-

ment included nebulised β_2 agonists, anticholinergics, and systemic corticosteroids in 3492 (93%), 1841 (49%), and 2252 (60%), respectively. According to severity classification, anticholinergics were used in 494 (51%), 913 (50%), and 434 (45%) of patients in life-threatening, severe, and mild to moderate exacerbations groups, respectively; corticosteroids were given in 666 (68%), 1117 (61%), and 468 (49%), respectively. The overall admission rate was 54.2%, and mean stay was 6.1 (SD 6.0) days. Patients were admitted in 747 (77%), 1018 (55%), and 278 (29%) of cases in life-threatening, severe, and mild to moderate groups, respectively. Three patients died in hospital. Interpretation: Acute asthma exacerbations are often life-threatening in patients who attend accident and emergency departments, and management of patients is not ideal, mainly because of underuse of corticosteroids and inappropriate admission rates according to severity.

Effect of Postpyloric Feeding on Gastroesophageal Regurgitation and Pulmonary Microaspiration: Results of a Randomized Controlled Trial—Heyland DK, Drover JW, MacDonald S, Novak F, Lam M. Crit Care Med 2001 Aug;29(8):1495–1501.

OBJECTIVE: To determine the extent to which postpyloric feeding reduces gastroesophageal regurgitation and pulmonary microaspiration in critically ill patients. DESIGN: Randomized trial. SETTING: A medical/surgical intensive care unit at a tertiary care hospital. PARTICIPANTS: Intensive care unit patients were expected to remain ventilated >72 hrs. We excluded patients with esophageal, gastric, or small bowel surgery in the last week and patients with overt or clinically significant gastrointestinal bleeding. We studied 33 patients; 42.4% were female, mean age (sd) was 59.2 (± 16.8) yrs, and mean Acute Physiology and Chronic Health Evaluation II score was 22.5 (7.8). INTERVENTIONS: Patients were randomized to gastric or postpyloric enteral feeds. Technetium 99-sulphur colloid was added to the feeds for 6 hrs of each of the first 3 days on study. MEASUREMENTS AND RESULTS: We sampled the oropharynx and trachea hourly for the 6 hrs per day that patients received radioisotope-labeled enteral feeds, and the level of radioactivity in these specimens was measured. We defined an episode of gastroesophageal regurgitation and microaspiration as an increase in radioactivity >100 counts per minute/g. Patients fed into the stomach had more episodes of gastroesophageal regurgitation (39.8% vs. 24.9%, p = 0.04) and trended toward more microaspiration (7.5% vs. 3.9%, p = 0.22) compared with patients fed beyond the pylorus. When the logarithmic mean of the radioactivity count was compared across groups, there was a trend toward an increase in gastroesophageal regurgitation (3.7 vs. 2.9 counts/g, p = 0.22) and a trend toward increased microaspiration (1.9 vs. 1.4 counts/g, p = 0.09) in patients fed into the stomach. Patients who had gastroesophageal regurgitation were much more likely to aspirate than patients who did not have gastroesophageal regurgitation (odds ratio: 3.2; 95% confidence interval: 1.36, 7.77). CONCLUSIONS: Feeding beyond the pylorus is associated with a significant reduction in gastroesophageal regurgitation and a trend toward less microaspiration.

Radiologic Determination of Intravascular Volume Status Using Portable, Digital Chest Radiography: A Prospective Investigation in 100 Patients—Ely EW, Smith AC, Chiles C, Aquino SL, Harle TS, Evans GW, Haponik EF. Crit Care Med 2001 Aug;29(8):1502–1512.

OBJECTIVE: To answer the following questions: Can the digital chest roentgenogram (CXR) be used to differentiate patients' volume status? Do clinical data alter radiologists' accuracy in interpreting the digital CXR? DESIGN: Prospective cohort study. SETTING: Nine adult intensive care units of a tertiary care medical center. PATIENTS: One hundred thirty-five consecutive patients with pulmonary artery catheters, of whom 35 were excluded because of unacceptable pulmonary artery occlusion pressure (PAOP) tracings. METHODS: Each patient had a portable, anteroposterior, supine digital CXR. Clinicians evaluated volume status and then measured hemodynamic data within 1 hr of the CXR. Digital CXRs were independently interpreted on two separate occasions (with and without clinical information) by three experienced chest radiologists, and these interpretations were compared with hemodynamic data. RESULTS: Of the 100 patients, 39 had PAOP >18 mm Hg, whereas 61 had PAOP <18 mm Hg. Radiologists' accuracy in differentiating volume status increased with incorporation of clinical data (56% without vs. 65% with clinical data, p = 0.009). Using objective receiver operating characteristic-derived cutoffs of 70 mm for vascular pedicle width and 0.55 for cardiothoracic ratio, radiologists' accuracy in differentiating PAOP >18 mm Hg from PAOP <18 mm Hg was 70%. The intrareader and the inter-reader correlation coefficients were very high. The likelihood ratio of the CXR in determining volume status using the objective vascular pedicle width and cardiothoracic ratio measures was 3.1 (95% confidence interval, 1.9–6.0), significantly higher than subjective CXR interpretations with and without clinical data (p <.001). CONCLUSIONS: Differentiating intravascular volume status with portable, supine, digital CXRs may be improved by using objective cutoffs of vascular pedicle width >70 mm and cardiothoracic ratio >0.55 or by incorporating clinical data.

Acute Cor Pulmonale in Acute Respiratory Distress Syndrome Submitted to Protective Ventilation: Incidence, Clinical Implications, and Prognosis—Vieillard-Baron A, Schmitt JM, Augarde R, Fellahi JL, Prin S, Page B, et al. Crit Care Med 2001 Aug;29(8):1551–1555.

CONTEXT: The incidence of acute cor pulmonale (ACP), a frequent and usually lethal complication of acute respiratory distress syndrome (ARDS) during traditional respiratory support, has never been re-evaluated since protective ventilation gained acceptance. OBJECTIVE: We performed a longitudinal transesophageal echocardiographic (TEE) study to determine whether this incidence, and its severe implications for prognosis, might have changed in our unit as we altered respiratory strategy. DESIGN: Prospective open clinical study. SETTING: Medical intensive care unit of a university hospital. PATIENTS: Seventy-five consecutive ARDS patients given respiratory support with airway pressure limitation (plateau pressure ≤ 30 cm H_2O). INTERVENTIONS: ACP was defined as a ratio of right ventricular end-diastolic area to left ventricular end-diastolic area in the long axis > 0.6 associated with septal dyskinesia in the short axis during TEE examination. RESULTS: Normal right ventricular function was present in 56 patients, whereas right ventricular dysfunction was observed in 19 patients after 2 days of respiratory support. ACP was associated with pulmonary artery hypertension, increased heart rate, and decreased stroke index. Significant impairment of left ventricular diastolic function was also seen. All echo-Doppler abnormalities were reversible in patients who recovered, and the mortality rate was the same in both groups (32%). However, ACP patients who recovered required a longer period of respiratory support. A multivariate analysis individualized P_{aCO_2} level as the sole factor independently associated with ACP, suggesting that ACP development in ARDS is influenced by the severity of lung damage and/or the respiratory strategy. CONCLUSION: Evaluation of right ventricular function by TEE in a group of 75 ARDS patients submitted to protective ventilation revealed the persistence of a 25% incidence of ACP, resulting in detrimental hemodynamic consequences associated with tachycardia. However, ACP was reversible in patients who recovered and did not increase mortality.

Repetitive High-Pressure Recruitment Maneuvers Required to Maximally Recruit Lung in a Sheep Model of Acute Respiratory Distress Syndrome—Fujino Y, Goddon S, Dolhnikoff M, Hess D, Amato MB, Kacmarek RM. Crit Care Med 2001 Aug;29(8):1579–1586.

OBJECTIVE: To compare the effects of two different recruitment maneuvers repeated multiple times on gas exchange lung injury, hemodynamic, and lung mechanics. DESIGN: Randomized prospective compar-

Every Intubation. Every Time.

During any intubation, the challenge of managing your patient's airway is significant. From the field to the ER and throughout the hospital, Nellcor® *Easy Cap® II* CO_2 Detectors help you meet that challenge by verifying correct endotracheal (ET) tube placement.

Establishing a cost-effective protocol to verify proper ET tube placement is more than an option, it's a necessity. Guidelines of the American Heart Association and the American Association for Respiratory Care, as well as an American Society of Anesthesiologists standard of care, state that carbon dioxide (CO_2) detection be an adjunct to clinical assessment when verifying correct ET tube placement.

Safe, simple and cost effective, the *Easy Cap II* CO_2 Detector offers breath-to-breath response. It quickly responds to exhaled CO_2 with a simple color change from purple to yellow, providing constant visual feedback for up to two hours.

Make *Easy Cap II* CO_2 Detectors part of your practice. Every intubation. Every time.

Call Customer Service at **800-635-5267** or visit our website at **www.nellcor.com.**

tyco Healthcare

Nellcor

© 2001 Nellcor Puritan Bennett Inc.
All rights reserved. B.f.0101-06/01

Easy Cap II

CO_2 Detectors

Inspiration

For the same breath-to-breath detection for patients up to 15 kg, ask for Pedi-Cap®.

Circle 108 on product information card

ison. SETTINGS: Animal research laboratory. SUBJECT: Nineteen fasted Hampshire sheep. INTERVENTIONS: In 15 27-kg sheep with saline lavage lung injury, we compared the effects of two recruitment maneuvers: 40 cm H_2O continuous positive airway pressure for 60 secs and 40 cm H_2O positive end-expiratory pressure with 20 cm H_2O pressure control, rate 10 breaths/min, inspiratory to expiratory ratio 1:1 for 2 mins. Each recruitment maneuver was repeated four times, every 30 mins after a 30-sec ventilator disconnection. An additional group received no recruitment maneuvers. Animals were assigned randomly to the three groups and ventilated with 20 cm H_2O positive end-expiratory pressure, pressure control 15 cm H_2O, rate 20 breaths/min, inspiratory to expiratory ratio 1:1, and F_{IO_2} 1.0 between recruitment maneuver periods. MEASUREMENTS AND MAIN RESULTS: Significant and marked increases in P_{aO_2} were observed in the pressure control recruitment maneuver group but only after the second recruitment maneuver. In both the control group and continuous positive airway pressure groups, P_{aO_2} did not significantly increase after any recruitment maneuver compared with baseline injury. There was a significant decrease in cardiac output immediately after some continuous positive airway pressure recruitment maneuvers and a significant increase in mean pulmonary artery pressure in both continuous positive airway pressure and pressure control groups immediately after recruitment maneuvers, but these changes resolved within 10 mins. There were no marked histologic differences between groups and no volutrauma. CONCLUSION: In this model, maximal lung recruitment was obtained with 40 cm H_2O positive end-expiratory pressure and 20 cm H_2O pressure control applied repetitively every 30 mins for 2 mins without physiologic or histologic harm. Multiple recruitment maneuvers in some animals were required for maximum effect.

Relative Roles of Vascular and Airspace Pressures in Ventilator-Induced Lung Injury—Hotchkiss JR Jr, Blanch L, Naveira A, Adams AB, Carter C, Olson DA, et al. Crit Care Med 2001 Aug;29(8):1593–1598.

OBJECTIVE: To determine whether elevations in pulmonary vascular pressure induced by mechanical ventilation are more injurious than elevations of pulmonary vascular pressure of similar magnitude occurring in the absence of mechanical ventilation. DESIGN: Prospective comparative laboratory investigation. SETTING: University research laboratory. SUBJECTS: Male New Zealand white rabbits. INTERVENTIONS: Three groups of isolated, perfused rabbit lungs were exposed to cyclic elevation of pulmonary artery pressures arising from either intermittent positive pressure mechanical ventilation or from pulsatile perfusion of lungs held motionless by continuous positive airway pressure. Peak, mean, and nadir pulmonary artery pressures and mean airway pressure were matched between groups (35, 27.4 ± 0.74, and 20.8 ± 1.5 mm Hg, and 17.7 ± 0.22 cm H_2O, respectively). MEASUREMENTS AND MAIN RESULTS: Lungs exposed to elevated pulmonary artery pressures attributable to intermittent positive pressure mechanical ventilation formed more edema (6.8 ± 1.3 vs. 1.1 ± 0.9 g/g of lung), displayed more perivascular (61 ± 26 vs. 15 ± 13 vessels) and alveolar hemorrhage (76 ± 11% vs. 26 ± 18% of alveoli), and underwent larger fractional declines in static compliance (88 ± 4.4% vs. 48 ± 25.1% decline) than lungs exposed to similar peak and mean pulmonary artery pressures in the absence of tidal positive pressure ventilation. CONCLUSIONS: Isolated phasic elevations of pulmonary artery pressure may cause less damage than those occurring during intermittent positive pressure mechanical ventilation, suggesting that cyclic changes in perivascular pressure surrounding extra-alveolar vessels may be important in the genesis of ventilator-induced lung injury.

Trends in Technology and the Future Intensive Care Unit—Craft RL. Crit Care Med 2001 Aug;29(8Suppl):N151-N158.

As advanced as today's critical care units are, changes in networks, computing platforms, instrumentation, human-machine interfaces, and software infrastructures and work being done in interoperability, process automation, and decision support all promise to alter both the structure and the operation of future critical unit settings. Although, as Yogi Berra said, "It's tough to make predictions, especially about the future," we can gain of a sense of the possibilities by studying emerging trends in each of these information technology-related areas. After describing notional physical and functional architectures for today's critical care units, this article provides a high-level overview of a number of trends in the areas listed above and provides the reader with starting points for further study. Although each of these trends may be fairly unremarkable when taken in isolation, when considered as a whole, the implications for critical care are profound. To that end, a final section of the article speculates on specific ways that these trends are likely to play themselves out in the context of tomorrow's critical care environments.

Computer-Assisted Learning in Critical Care: From ENIAC to HAL—Tegtmeyer K, Ibsen L, Goldstein B. Crit Care Med 2001 Aug; 29(8Suppl):N177-N182.

Computers are commonly used to serve many functions in today's modern intensive care unit. One of the most intriguing and perhaps most challenging applications of computers has been to attempt to improve medical education. With the introduction of the first computer, medical educators began looking for ways to incorporate their use into the modern curriculum. Prior limitations of cost and complexity of computers have consistently decreased since their introduction, making it increasingly feasible to incorporate computers into medical education. Simultaneously, the capabilities and capacities of computers have increased. Combining the computer with other modern digital technology has allowed the development of more intricate and realistic educational tools. The purpose of this article is to briefly describe the history and use of computers in medical education with special reference to critical care medicine. In addition, we will examine the role of computers in teaching and learning and discuss the types of interaction between the computer user and the computer.

The eICU: It's Not Just Telemedicine—Celi LA, Hassan E, Marquardt C, Breslow M, Rosenfeld B. Crit Care Med 2001 Aug;29(8Suppl):N183-N189.

Intensive care units (ICUs) are major sites for medical errors and adverse events. Suboptimal outcomes reflect a widespread failure to implement care delivery systems that successfully address the complexity of modern ICUs. Whereas other industries have used information technologies to fundamentally improve operating efficiency and enhance safety, medicine has been slow to implement such strategies. Most ICUs do not even track performance; fewer still have the capability to examine clinical data and use this information to guide quality improvement initiatives. This article describes a technology-enabled care model (electronic ICU, or eICU) that represents a new paradigm for delivery of critical care services. A major component of the model is the use of telemedicine to leverage clinical expertise and facilitate a round-the-clock proactive care by intensivist-led teams of ICU caregivers. Novel data presentation formats, computerized decision support, and smart alarms are used to enhance efficiency, increase effectiveness, and standardize clinical and operating processes. In addition, the technology infrastructure facilitates performance improvement by providing an automated means to measure outcomes, track performance, and monitor resource utilization. The program is designed to support the multidisciplinary intensivist-led team model and incorporates comprehensive ICU re-engineering efforts to change practice behavior. Although this model can transform ICUs into centers of excellence, success will hinge on hospitals accepting the un-

That's Texas Health Resources

★RESPIRATORY THERAPIST★
★ NICU RESPIRATORY THERAPIST★
(Full-time, part-time & variable shifts)

At Texas Health Resources, we recognize our Respiratory Therapists as an integral part of our patient care team. Our therapists assist physicians in state-of-the-art clinical laboratories, operating rooms, diagnostic centers, and extended care facilities to provide the best respiratory care possible. This is why we offer tremendous challenges and rewards, plus the support of an organization that puts the best technology, resources and work environment at your disposal. Join Texas Health Resources and see why we offer you more to feel good about!

Our goal is to attract and keep the brightest professionals. That is why we offer competitive pay, flexible health plans, paid time off, flexible scheduling, accelerated matching 401(k) plan and tuition reimbursement. In addition, we offer employee wellness programs, referral bonuses, the opportunity to work in a variety of environments including large metroplex hospitals or urban community hospitals and a host of other great benefits all designed to make working for Texas Health Resources a highly satisfying and rewarding experience.

Planning & Placement, Attn: David Hall
611 Ryan Plaza Drive, Suite 200, Arlington, TX 76011
1-866-JOBS THR, Fax: 1-866-889-8978
www.TexasHealth.org
Apply Online: www.JobsTHR.com

TEXAS HEALTH RESOURCES℠

Harris Methodist Hospitals • Arlington Memorial Hospital • Presbyterian Healthcare System

Texas Health Resources is an equal opportunity employer which values and celebrates diversity at all levels of our organization.

Circle 104 on product information card

derlying value proposition and physicians being willing to change established practices.

Measuring the Impact of New Technology: An Outcomes-Based Approach—Sachdeva RC. Crit Care Med 2001 Aug;29(8Suppl):N190-N195.

In the current era of decreasing resources, many healthcare organizations are under increasing pressure to evaluate new technology. Advances and innovations in healthcare technology are instrumental in reshaping the healthcare system and in impacting the practice of medicine, including critical care. Healthcare organizations are faced with the following four questions related to adopting a new technology: 1) Should the organization invest in this technology? 2) What are the associated benefits and risks of the capital investment? 3) What is the impact on patient outcomes as a result of adopting the technology? 4) What is the return on investment to the organization? These issues represent challenging areas for the researcher, clinician, manager, and policy maker. New techniques from the business and outcomes research arenas allow for the development of quantitative and qualitative models to facilitate answering these questions. By integrating business and clinical considerations, these models can impact policy at two levels: 1) by identifying optimal capital expenditure decisions for individual healthcare organizations, it can provide a significant competitive advantage for an organization; and 2) by identifying optimal health policies related to technology at a national and international health level, it can impact the healthcare systems and patient outcomes in a favorable manner.

Online Personal Medical Records: Are They Reliable for Acute/Critical Care?—Schneider JH. Crit Care Med 2001 Aug;29(8Suppl):N196-N201.

OBJECTIVE: To provide an introduction to Internet-based Online Personal Medical Records (OPMRs), to assess their use and limitations in acute/critical care situations, and to identify potential improvements that could increase their usefulness. DESIGN: A review of publicly available Internet-based OPMRs conducted in April 2001. DATA SOURCES: Twenty-nine OPMR sites were identified in March 2000 using ten Internet search engines with the search term "Personal Medical Records." Through 2000 and 2001, an additional 37 sites were identified using lists obtained from trade journals and through the author's participation in standards-setting meetings. MEASUREMENTS: Each publicly available site was reviewed to assess suitability for acute/critical care situations using four measures developed by the author and for general use using eight measures developed in a standards-setting process described in the article. RESULTS: Of the 66 companies identified, only 16 still offer OPMRs that are available to the public on the Internet. None of these met all of the evaluation measures. Only 19% had rapid emergency access capabilities and only 63% provided medical summaries of the record. Security and confidentiality issues were well addressed in 94% of sites. Data portability was virtually nonexistent because all OPMRs lacked the ability to exchange data electronically with other OPMRs, and only two OPMRs permitted data transfer from physician electronic medical records. Controls over data accuracy were poor: 81% of sites allowed entry of dates for medical treatment before the patient's date of birth, and one site actually gave incorrect medical advice. OPMRs were periodically inaccessible because of programming deficiencies. Finally, approximately 40 sites ceased providing OPMRs in the past year, with the probable loss of patient information. CONCLUSIONS: Most OPMRs are not ready for use in acute/critical care situations. Many are just electronic versions of the paper-based health record notebooks that patients have used for years. They have, however, great promise and, with further development, could form the basis of a new medical record system that could contribute to improving the quality of medical care.

End-of-Life Decisions in Cancer Care—Price KJ, Kish SK. Crit Care Clin 2001 Jul;17(3):805–811.

End-of-life decisions in critically ill patients with cancer are often complex and fraught with emotion. End-of-life care involves a multidisciplinary approach that takes into account the patient and family's desires and the goals of therapy. Decisions regarding the use of life-support technology at the end of life encompass an outcomes and goal-oriented approach. Ethical, medical, legal, and economic issues should be considered in the assessment of life-support technologies and directives for their appropriate use in the ICU.

Intensive Care, Mechanical Ventilation, Dialysis, and Cardiopulmonary Resuscitation: Implications for the Patient with Cancer—Groeger JS, Aurora RN. Crit Care Clin 2001 Jul;17(3):791–803.

The broad range in mortality rates seen in the critically ill cancer population reflects the fact that cancer is a heterogeneous disease, affecting a heterogeneous population at different stages of care. Patients, families, and physicians frequently agonize about the utility of CPR and ICU care and whether this care should be offered. Understanding the goals of care, respecting autonomy, and knowing the likelihood of benefits and burdens of these interventions are critical in making these difficult decisions.

Acute Respiratory Failure in Critically Ill Patients with Cancer: Diagnosis and Management—Pastores SM. Crit Care Clin 2001 Jul;17(3):623–646.

Respiratory failure remains a common cause of admission to the ICU for patients with cancer, regardless of the nature of malignancy. The diagnosis and management of ARF in patients with cancer poses special challenges to the intensivist. Depending on the type of cancer, the degree of immunosuppression, underlying comorbidities, the modality of cancer treatment, progression or spread of underlying cancer, and disease- or therapy-associated complications are the most common causes of ARF in these patients. Despite significant advances in antineoplastic therapies and supportive management in the ICU, the mortality rate of patients with cancer with ARF remains high. Severity-of-illness scoring systems and mortality probability models, although useful in discriminating between survivors and nonsurvivors in large groups of critically ill patients, should not be used alone to justify reluctance in admitting individual patients with cancer with potentially reversible respiratory failure to the ICU. Close collaboration between oncologists and intensivists will ensure the establishment of clear goals and direction of treatment for every patient with cancer who requires mechanical ventilation.

Mechanistic Scheme and Effect of "Extended Sigh" as a Recruitment Maneuver in Patients with Acute Respiratory Distress Syndrome: A Preliminary Study—Lim CM, Koh Y, Park W, Chin JY, Shim TS, Lee SD, et al. Crit Care Med 2001 Jun;29(6):1255–1260.

OBJECTIVE: To devise a new form of sigh ("extended sigh") capable of providing a sufficient recruiting pressure x time, and to test it as a recruitment maneuver in patients with acute respiratory distress syndrome. DESIGN: Prospective uncontrolled clinical trial. SETTING: Medical intensive care unit of a university-affiliated hospital. PATIENTS: Twenty consecutive patients diagnosed with acute respiratory distress syndrome (18 men, 2 women, age 59 ± 10 yrs). INTERVENTIONS: From baseline settings of tidal volume (V_T) 8 mL/kg and positive end-expiratory pressure (PEEP) 10 cm H_2O on volume control mode with the high pressure limit at 40 cm H_2O, the V_T-PEEP values were changed to 6–15, 4–20, and 2–25, each step being 30 secs (inflation phase). After V_T-PEEP 2–25, the mode was switched to continuous positive airway pressure of 30 cm H_2O for a duration of 30 secs (pause), after which the baseline setting was resumed following the reverse sequence of inflation

Set Your Career With America's Best Medical Staffing Company!

* 24 Hour Support
*Short & Long Term Assignments
*Desirable Locations
*Workman's Compensation
*Top-Pay & Meal Allowance
*Pre-Paid Travel
*Private Lodging & Utilities
*Free Rental Car
*Immediate Health Insurance
*Shift Differentials
*Licensure Assistance
*Direct Deposit

RRT*CRT*POLY

Contact:
Glenda Collins
800-461-1815
glenda@technetmedical.com
Or
Misti Herrera
800-461-1815
misti@technetmedical.com

Call
Tech Net Medical
To Set Your Career Today!
800-461-1815
Fax 888-782-3358

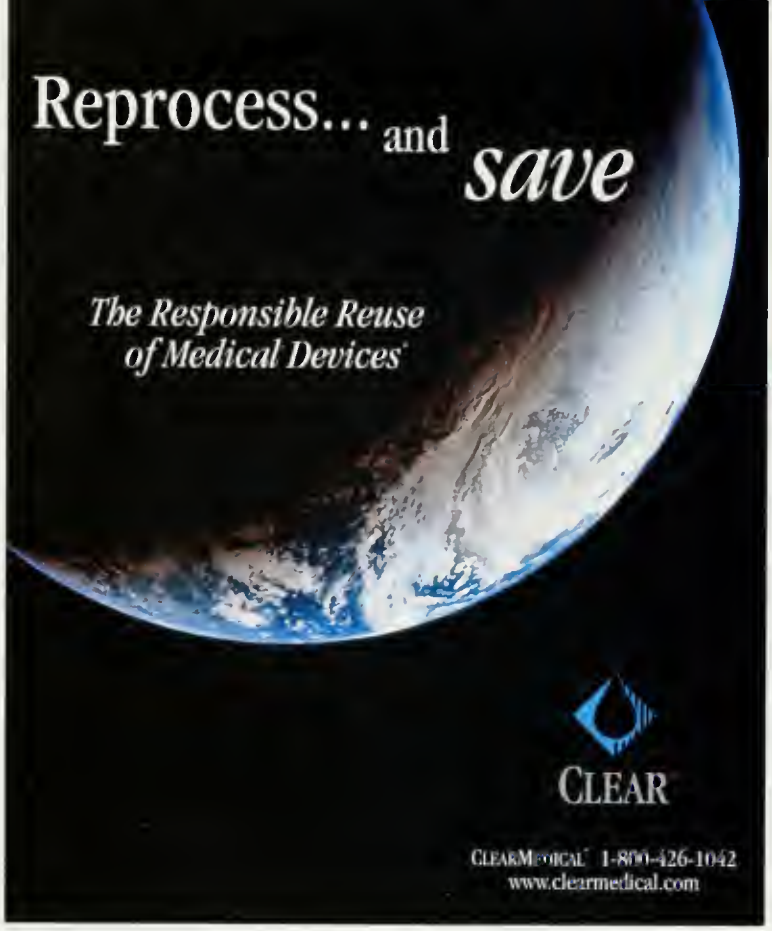
Check Us Out On The Web!
www.technetmedical.com
info@technetmedical.com

TNM LLC

Tech Net Medical, LLC
800-461-1815
Fax: 888-782-3358

The Heart Beat Of Healthcare

Circle 113 on product information card



Circle 128 on product info card

(deflation phase). This extended sigh was performed twice with 1 min of baseline ventilation between. MEASUREMENTS AND RESULTS: Airway pressures and hemodynamic parameters were traced at each step during the extended sigh. Arterial blood gases and physiologic parameters were determined before the extended sigh (pre-extended sigh), at 5 mins after two extended sighs (post-extended sigh), and then every 15 mins for 1 hr. In our average patient, the recruiting pressure x time of the inflation phase was estimated to be 32.8–35.4 cm H_2O x 90 secs. Compared with the inflation phase, inspiratory pause pressure of the deflation phase was lower at V_T-PEEP 6–15 (28.9 ± 2.7 cm H_2O vs. 27.3 ± 2.8 cm H_2O) and 4–20 (31.8 ± 2.9 cm H_2O vs. 31.1 ± 2.9 cm H_2O; both $p < 0.05$). Compared with pre-extended sigh, P_{aO_2} (81.5 ± 15.3 mm Hg vs. 104.8 ± 25.0 mm Hg; $p < 0.001$) and static respiratory compliance both increased post-extended sigh (27.9 ± 7.9 mL/cm H_2O vs. 30.2 ± 9.7 mL/cm H_2O; $p = 0.009$). Improvement in these parameters was sustained above pre-extended sigh for the duration of the study. Major hemodynamic or respiratory complications were not noted during the study. CONCLUSION: We present a new form of sigh (i.e., extended sigh) capable of achieving an augmented recruiting pressure x time through a prolonged inflation on a gradually increased end-expiratory pressure. In view of the sustained effect and absence of major complications in our patients, extended sigh could be a useful recruitment maneuver in acute respiratory distress syndrome.

Patient Satisfaction Associated with Correct Identification of Physician's Photographs—Francis JJ, Pankratz VS, Huddleston JM. Mayo Clin Proc 2001 Jun;76(6):604–608.

OBJECTIVE: To determine whether placement of photographs of physicians in hospital rooms improves patients' satisfaction with their medical care. PATIENTS AND METHODS: This is a prospective, controlled study of 224 patients admitted to general internal medicine services in a teaching hospital. The intervention consisted of photographs (8 x 10 in) of attending and resident physicians displayed in the patients' rooms. Before dismissal, patients completed a survey that required them to match names with photographs of physician caregivers and included patient satisfaction questions. The primary outcome was whether patients who had photographs in their hospital room would correctly identify more physicians than those with no photographs in their room. RESULTS: The presence of photographs on the hospital wall was associated with a significant improvement in the number of physicians identified correctly (odds ratio [OR], 1.83; 95% confidence interval [CI], 1.47–2.27; $p < 0.001$). The percentage of physicians that patients identified by correctly matching their physicians' names to their photographs was significantly associated with satisfaction with physician responsiveness (OR, 1.19; 95% CI, 1.01–1.40; $p = 0.03$) and with the way in which physicians addressed questions regarding medical care (OR, 1.23; 95% CI, 1.05–1.44; $p = 0.05$). CONCLUSIONS: Patients who had photographs of their physicians on the wall of their hospital room were able to identify correctly a larger number of physicians on their team compared with patients who had no photographs. Patient satisfaction was related to the number of physicians' photographs that patients could identify correctly.

A Guide to the Diagnosis and Treatment of Occupational Asthma—Rabatin JT, Cowl CT. Mayo Clin Proc 2001 Jun;76(6):633–640.

Occupational asthma is the most prevalent form of occupational lung disease in industrialized nations. As increasing numbers of new chemicals are produced and new manufacturing processes are introduced, the variety of environments in which individuals may become exposed to respiratory sensitizers and irritants makes diagnosing and treating this illness even more challenging. In addition to adverse pulmonary effects, the diagnosis of occupational asthma may bring with it negative social and financial implications that may ultimately affect the patient's quality

Meet JCAHO Requirements – Demonstrate Employee Competence with

Diagnostic Training and Competence Assessment Manual for Pulmonary & Noninvasive Cardiology

You no longer have to rely on your experience to help employees demonstrate competence in pulmonary and noninvasive cardiology. Now, there's the new Diagnostic Training and Competence Assessment Manual for Pulmonary and Noninvasive Cardiology on CD-ROM.

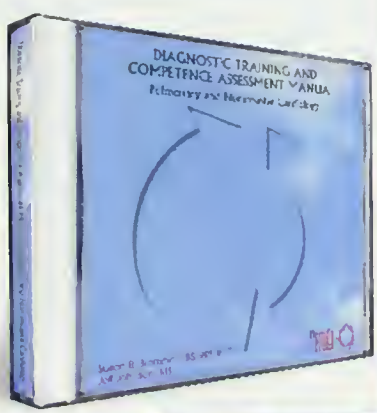
Ideal for use in course development, training, orientation, and competence assessment for individuals in the laboratory setting.

Pulmonary Diagnostics Section features: quality control, diffusing capacity, whole body plethysmography, indirect calorimetry, arterial blood gas sampling, bronchoscopy, spirometry, static lung volumes, bronchial provocation testing, pulse oximetry, venipuncture, technologist-driven protocols.

Noninvasive Cardiology Section features: electrocardiography, cardiopulmonary stress testing, transtelephonic event monitoring, transtelephonic pacemaker evaluation, graded exercise testing, ambulatory electrocardiography, high resolution signal-average ECG.

Requirements: 486 or Pentium class computer with Windows 301, Windows 95 or higher and 8 MB of available hard drive space and a CD ROM drive.

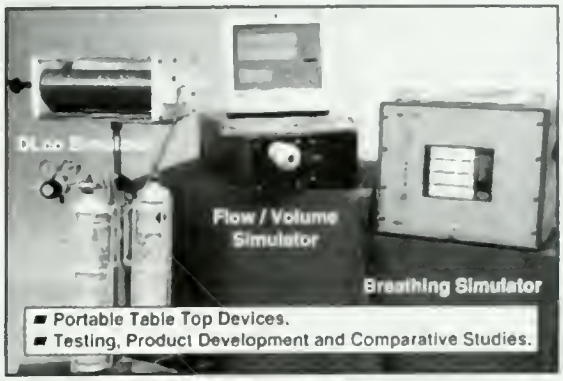
ITEM PA99 $267.00
(Nonmembers $289.00)
Shipping & Handling $16.25



To order call 972.406.4663
and charge your order to a MasterCard, Visa, or purchase order.

Shop online at
http://store.yahoo.com/aarc

NEW! Hans Rudolph NEW!
Introduces a Family of
LUNG SIMULATORS
For Your Simulation Needs


Flow / Volume Simulator
Breathing Simulator
▰ Portable Table Top Devices.
▰ Testing, Product Development and Comparative Studies.

DLco Simulator with EasyLab QC™ Software
- Checks accuracy and variability of Single-Breath Carbon Monoxide Diffusing Capacity (DLco) Devices
- Defines, Charts, Graphs, and Compares the DLco Devices with biological control subjects and projected values

Flow / Volume Simulator
- Generates the ATS Waveforms and Custom Waveforms
- Modes for Spirometry, Steady State Flow and Continuous Breathing Waveforms

Breathing Simulator
- A spontaneously breathing Lung Model.
- Simulates spontaneous and passive patients

HANS RUDOLPH, inc. CE ISO 9001 EN 46001
MAKERS OF RESPIRATORY VALVES SINCE 1938
TEL: (816) 363-5522 USA & CANADA (800) 456-6695
FAX: (816) 822-1414 E-Mail: hri@rudolphkc.com www.rudolphkc.com
7205 CENTRAL, KANSAS CITY, MISSOURI 64114 U.S.A.

Circle 159 on product information card

NEW! 2ND EDITION
Respiratory Care Patient-Driven Protocols

Now Includes Pediatric Protocols

An excellent resource in the processes of developing, implementing, or refining care plans. Helps you improve patient care and control costs. Features 29 complete protocols including: Oxygen, Oximetry, MDI, SVN, PEP, Thoracoscopy, IPPB, Extubation, Secretion Management, Weaning, Pediatrics, and others. Also includes an expanded and valuable introduction on how to implement PDPs in your facility. Softcover. 257 pages. Second Edition. Published in 2001.

Item # PA8012-A $85.00 ($99.00 Nonmembers).
Add $9.25 for shipping and handling.

NEW - Pediatric Metered Dose Inhaler Protocol (Ages 5-12)
NEW - Simple Weaning Protocol for Pediatrics
NEW - Introduction Contains an Overview of PDPs and Operational Costs

Order Online at http://store.yahoo.com/aarc/
MasterCard • Visa • Purchase Order

Daedalus Enterprises, Inc.
P.O. Box 29686 • Dallas, TX 75229 • (972) 406-4663 • Fax (972) 484-2720

Visit www.aarc.org

of life. For this reason, it is important for clinicians to recognize work-related respiratory symptoms early on in their course, maintain a high clinical suspicion for an occupational cause in the diagnostic work-up of asthma, and have a high degree of certainty in the diagnosis. While a number of classification schemes have been proposed to simplify the diagnostic approach to occupational asthma, the inciting factors typically involve sensitization (often by an IgE mechanism), direct airway inflammation, various pharmacologic responses, or irritant reflex pathways. Clinicians must first document the presence of asthma, then establish a relationship between asthma and the work-place. The occupational history is the key diagnostic tool, and clinical suspicions may be evaluated further by serial peak expiratory flow measurements, nonspecific hypersensitivity challenges with histamine or methacholine, collaboration with industrial/occupational hygienists to obtain workplace exposure measurements, and specific challenge testing at tertiary referral centers providing specialized laboratories. Removal from the inciting exposure is the mainstay of therapy, and pharmacologic treatment of patients with occupational asthma is similar to the treatment of patients with other forms of asthma.

Medical Advice for International Travelers—Virk A. Mayo Clin Proc 2001 Aug;76(8):831–840.

Each year, approximately 30 to 40 million Americans travel outside the United States. Although the most popular destinations are Europe, Central America, and the Caribbean, travel to Africa and Asia is increasing substantially. International travel, particularly to developing countries, can be associated with the risk of infectious and noninfectious diseases. These risks can be decreased, eliminated, or modified with vaccinations, prophylactic medications, and education. Optimally, pretravel advice must be individualized to a person's medical history, itinerary, and risk behavior. In addition to risk assessment-based immunizations, issues such as traveler's diarrhea, malaria prophylaxis, sexually transmitted diseases, and management of underlying medical problems must form a part of pretravel management. Adventure or prolonged travel or persons with underlying medical diseases such as insulin-dependent diabetes mellitus, transplantation, immunodeficiencies, and dialysis warrant additional preventive measures. This review primarily updates pretravel management of adults.

Fast-Tracking Pulmonary Resections—Cerfolio RJ, Pickens A, Bass C, Katholi C. J Thorac Cardiovasc Surg 2001 Aug;122(2):318–324.

OBJECTIVE: We streamlined our care after pulmonary resection for quality and cost-effectiveness. METHODS: A single surgeon performed 500 consecutive pulmonary resections through a thoracotomy over a 2(3/4)-year period in a university setting. Patients were extubated in the operating room and sent directly to their hospital room. Chest tubes were placed to water seal and removed on postoperative day 2 if there was no air leak and drainage was less then 400 mL/d. Epidural catheters were used and removed by postoperative day 2. The plan for each day and discharge on postoperative day 3 or 4 was reviewed with the patients and families daily during rounds. The patient went home the day the last chest tube was removed. Persistent air leaks were treated with Heimlich valves. RESULTS: There were 500 patients (338 men), with a median age of 58 years (range, 3–87 years). Of these patients, 293 had pre-existing conditions. Seventy-three (15%) patients had been denied operations by at least one other surgeon. Four hundred nineteen (84%) patients had successful placement of a functioning preoperative epidural catheter. Pneumonectomy was performed in 32 (6%) patients, segmentectomy was performed in 16 (3%) patients, and lobectomy, sleeve lobectomy, and/or bilobectomy was performed in 194 (39%) patients. Nonanatomic resections were performed for metastasectomy. This included a single wedge resection in 161 (32%) patients and multiple wedge resections in 97 (19%) patients. A total of 482 (96%) patients were extubated in the operating room, and 380 (76%) patients were sent to their hospital room. The remaining 120 patients went to the intensive care unit for a median of 1 day (range, 1–41 days). Complications occurred in 107 (21%) patients, and operative mortality was 2.0%. Median day of discharge was postoperative day 4 (range, 2–119 days). A total of 327 (65%) patients left the hospital on postoperative day 4 or sooner. By survey, 97% of patients had excellent or good satisfaction with their care at hospital discharge, and 91% were extremely happy or satisfied at the 2-week follow-up contact. CONCLUSIONS: Most patients who undergo elective pulmonary resection can be extubated immediately after the operation, go directly to their room and avoid the intensive care unit, be discharged on postoperative day 3 or 4, and have minimal morbidity and mortality with high satisfaction both at discharge and at the 2-week follow-up contact. Techniques that seem to accomplish this include the following: the use of a water seal, removal of epidural catheters on postoperative day 2, early chest tube management, treatment of persistent air leaks with Heimlich valves, and daily reinforcement of the planned events for each day, as well as on the date of discharge with the patients and their families.

Respiratory Distress Syndrome in the Newborn: Role of Oxidative Stress—Gitto E, Reiter RJ, Karbownik M, Xian-Tan D, Barberi I. Intensive Care Med 2001 Jul;27(7):1116–1123.

Reactive oxygen and nitrogen species are generated by several inflammatory and structural cells of the airways. These oxidant species have important effects on a variety of lung cells as regulators of signal transduction, activators of key transcription factors and modulators of gene expression and apoptosis. Thus, increased oxidative stress accompanied by reduced endogenous antioxidant defenses may play a role in the pathogenesis of a number of inflammatory pulmonary diseases, including respiratory distress syndrome (RDS) in the newborn. There obviously are conflicting reports on the effect of oxygen, ventilation and nitric oxide (NO) on RDS and, thus, the question arises as what the neonatologist should do when confronted with a newborn with RDS. Clearly, utilizing lung protective strategies requires compromises between gas exchange goals and potential toxicities associated with over-distension, derecruitment of lung units and high oxygen concentrations. The results discussed in this brief review suggest rigorous clinical tests with antioxidants which may help to define the mechanisms associated with RDS and which could lead to new treatment strategies.

Acute Respiratory Distress Syndrome Among Trauma Patients: Trends in ICU Mortality, Risk Factors, Complications and Resource Utilization—Navarrete-Navarro P, Rodriguez A, Reynolds N, West R, Habashi N, Rivera R, et al. Intensive Care Med 2001 Jul;27(7):1133–1140.

OBJECTIVE: To evaluate trends in mortality and related factors among trauma patients who developed acute respiratory distress syndrome (ARDS). STUDY: Observational study based on data prospectively gathered in computerized trauma registry. SETTING: Trauma intensive care unit (ICU) of 48 beds in level I trauma center. PATIENTS: All trauma patients with ARDS admitted during 1985–87 (486, group 1 [G1]) and 1993–95 (552, group 2[G2]). METHODS: ARDS was defined by American-European Consensus Conference criteria and the need for 48 h or more on mechanical ventilation with F_{IO_2} greater than 0.50 and PEEP of more than 5 cm H_2O. Demographics, severity score, injury-admission delay time, first 24-h transfusion and septic and organ system failure complications were independent variables. ICU mortality was the dependent variable. ICU length of stay (LOS) and life support techniques were considered. Respiratory and renal support strategies were different in the two time periods. RESULTS: Mortality decreased over the period (G1: 29.2% vs G2: 21.4%, $p < 0.04$), in patients aged both over and under 65 years. Multivariate analysis showed mortality was related to age, severity and time period (G1 1.68-fold that in G2) and that the greater G1 mor-

MANAGE *your* ASTHMA, REACH *your* PEAK

Help your patients manage their asthma for peak performance in every part of their lives. Asthma management products from Ferraris are designed to encourage patient compliance. Our monitoring, delivery and training devices are convenient, portable and, most importantly, reliable and effective. Ferraris products, along with your professional expertise, help your patients to establish and maintain their asthma management routines.

FERRARIS

your **PARTNER** *in*
ASTHMA MANAGEMENT

POCKET PEAK™
PEAK FLOW METER

AIRZONE™
PEAK FLOW METER

POCKET CHAMBER™ & POCKET SPACER™
AEROSOL HOLDING CHAMBERS

IN-CHECK DIAL®
TRAINING PRODUCT

Ferraris also offers the MiniWright™ Standard and AFS models as part of our full line of peak flow meters.

For more information call:
1-800-205-7187

FERRARIS MEDICAL, INC.
4 Centre Drive
Orchard Park, NY 14127 U.S.A.
www.ferrarismedicalusa.com
email: info@ferrarisny@aol.com

Circle 130 on product information card

tality was related to more renal failure and hematologic failure/dysfunction. ICU LOS decreased from 31.7±26.7 days (G1) to 27.3±22 days (G2) ($p < 0.003$). CONCLUSIONS: Mortality among trauma patients with ARDS declined over the 8 years studied and was associated with less organ failure. This reduction was probably the result of new approaches to mechanical ventilation, renal failure replacement and vasoactive drug therapy.

Mechanical Ventilation in Patients with Acute Ischemic Stroke: Survival and Outcome at One Year—Santoli F, De Jonghe B, Hayon J, Tran B, Piperaud M, Merrer J, Outin H. Intensive Care Med 2001 Jul; 27(7):1141–1146.

OBJECTIVE: To assess the prognosis of patients with acute ischemic stroke who require mechanical ventilation and to determine early factors influencing mortality. DESIGN: Prospective observational study. SETTING: Medical intensive care unit with a cerebrovascular emergency unit in a university-affiliated hospital. PATIENTS: Fifty-eight consecutive patients (mean age 65±13 years) requiring mechanical ventilation in the early course of an acute ischemic stroke. MEASUREMENTS AND RESULTS: Clinical data were recorded before intubation according to a standardized procedure. Mortality and functional outcome were assessed after a 1-year follow-up. Mechanical ventilation was started within 48 h after admission in 53 patients (91.4%). The mean duration of ventilation was similar in survivors (9.7±9.0 days) and non-survivors (8.6±8.7 days). Mortality was 72.4% at 1 year. Among the 16 survivors, none were in a persistent vegetative state and 11 had a Barthel index of 60, reflecting good functional status. Bilateral absence of corneal reflex and bilateral absence of pupillary light reflex had a positive predictive value of death of 1 (95% CI 0.78–1.00 and 0.74–1.00, respectively). After Cox regression analysis, presence of stupor or coma (OR 2.6, 95% CI 1.5–5.0), bilateral absence of corneal reflex before intubation (OR 3.4, 95% CI 1.4–8.7) and presence of ischemic cardiopathy (OR 2.8, 95% CI 1.4–5.5) were independent predictors of mortality. CONCLUSIONS: Systematic withholding of endotracheal intubation in patients with AIS is not recommended. Careful and rigorous neurologic examination, including assessment of brain stem reflexes, might help to identify patients with a very high probability of death despite mechanical ventilation.

The Development of Ventilator-Associated Pneumonia Does Not Change Aspects of Mechanical Ventilation—Dennesen PJ, Van der Ven AJ, Van der Geest S, Ramsay G, Bonten MJ. Intensive Care Med 2001 Jul;27(7):1158–1163.

OBJECTIVE: To evaluate whether the development of ventilator-associated pneumonia (VAP) is associated with changes in ventilation parameters. DESIGN: Matched case-control study. SETTING: Mixed intensive care unit of a university hospital. PATIENTS: From a large database we selected 33 patients with VAP, diagnosed with quantitative cultures of bronchoscopically obtained specimens. In addition, 33 other mechanically ventilated patients who did not develop VAP were selected (controls). Patients with VAP and controls were matched on seven variables representing severity of illness: duration of ventilation until matching, diagnosis on admission, renal function, liver function, preceding infection, preceding surgery and immunosuppressive therapy. Each patient with VAP was matched to a single control. Variables regarding type and mode of ventilation and interpretation of chest radiographs were not included in the matching procedure. MEASUREMENTS AND RESULTS: Characteristics of mechanical ventilation (mode of ventilation, tidal volume, expired minute ventilation, peak airway pressures, mean airway pressures, level of positive end-expiratory pressure, arterial oxygen tension(P_{aO_2})/fractional inspired oxygen (F_{IO_2}) ratio), were compared on the day of diagnosis of VAP (or matching for controls) and 2 and 4 days before. Although there was a significant difference in P_{aO_2}/F_{IO_2} ratios between cases and controls on the day of diagnosis of VAP, the change in P_{aO_2}/F_{IO_2} ratios during the days of study were not statistically different between patients developing VAP and controls. No significant differences were found for any of the other variables of ventilation at any of the three time points studied, nor were there significant differences in changes of these parameters within individual patients. CONCLUSIONS: Characteristics and parameters of mechanical ventilation are not influenced by the development of VAP. It is, therefore, unlikely that these variables are useful in the diagnostic work-up of VAP.

Validity of an Abbreviated Indirect Calorimetry Protocol for Measurement of Resting Energy Expenditure in Mechanically Ventilated and Spontaneously Breathing Critically Ill Patients—Petros S, Engelmann L. Intensive Care Med 2001 Jul;27(7):1164–1168.

OBJECTIVE: To test a short indirect calorimetry protocol with five stable 1-min readings (5-min steady state) against the commonly used protocol of 30 1-min readings (30-min steady state) in critically ill patients with various modes of ventilation. DESIGN: A prospective clinical study. SETTING: A medical ICU of a university hospital. SUBJECTS: Forty-six mechanically ventilated patients (group A and B), and 16 spontaneously breathing patients (group C). INTERVENTION: Indirect calorimetry with the Deltatrac II MBM-200 Metabolic Monitor. RESULTS: Mechanically ventilated patients were classified into group A (controlled) and B (assisted) depending on the ventilation mode. All patients in group A, but only 48.8% of those in group B, received some form of analgosedation, and the doses were significantly higher in group A. The 30-min steady state test was 100.0%, 83.7%, and 75.0% successful in group A, B, and C, respectively. The corresponding rate for the 5-min steady state test was 100.0%, 81.4%, and 100.0%, respectively. The coefficient of determination (r^2) for resting energy expenditure between the two protocols ranged between 0.972 and 0.994. The time required to collect the 5-min steady state data was 5.5±1.1, 9.9±5.7, and 6.5±3.3 min for group A, B, and C, respectively. CONCLUSION: Indirect calorimetry with 5-min steady state test correlated very well with the 30-min steady state test in both mechanically ventilated and spontaneously breathing patients. The time required varies depending on the mode of ventilation, and it is influenced by the level of sedation in mechanically ventilated patients. The abbreviated protocol may be more acceptable to spontaneously breathing patients.

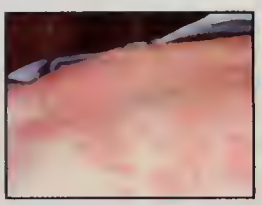
Improved Asthma Control with Budesonide/Formoterol in a Single Inhaler, Compared with Budesonide Alone—Zetterstrom O, Buhl R, Mellem H, Perpina M, Hedman J, O'Neill S, Ekstrom T. Eur Respir J 2001 Aug;18(2):262–268.

Budesonide/formoterol in a single inhaler was compared with budesonide alone, and with concurrent administration of budesonide and formoterol from separate inhalers, in patients with asthma, not controlled with inhaled glucocorticosteroids alone. In this 12-week, double-blind, randomized, double-dummy study, 362 adult asthmatics (forced expiratory volume in one second 73.8% of predicted, inhaled glucocorticosteroid dose 960 $\mu g \times day^{-1}$) received single inhaler budesonide/formoterol (Symbicort Turbuhaler) 160/4.5 μg, two inhalations b.i.d., or corresponding treatment with budesonide, or budesonide plus formoterol via separate inhalers. There was a greater increase in morning peak expiratory flow (PEF) with single-inhaler (35.7 $L \times min^{-1}$) and separate-inhaler (32.0 $L \times min^{-1}$) budesonide and formoterol, compared with budesonide alone (0.2 $L \times min^{-1}$; $p<0.001$, both comparisons); the effect was apparent after 1 day ($p<0.001$ versus budesonide, both comparisons). Similarly, evening PEF, use of rescue medication, total asthma symptom scores and percentage of symptom-free days improved more with both single inhaler and separate inhaler therapy than with budesonide alone, as did asthma control days (approximately 15% more, $p<0.001$ versus budesonide, both comparisons, with a marked increase in the first week). All treatments were well tolerated and the adverse event profile was similar in all

SAFER IS BETTER.

HY•TAPE® LATEX FREE.
SAFER FOR PATIENTS & HEALTHCARE PROFESSIONALS.

Hy•Tape features all the benefits of The Original Pink Tape®, plus it is now latex free. With Hy•Tape Latex Free every patient, even those who are latex-sensitive, can benefit from our zinc oxide formula that soothes the most delicate skin. Just like the original, Hy•Tape Latex Free removes painlessly, yet adheres safely and securely. Waterproof and washable, it is perfect for extended wear. Available in a variety of sizes and packaging options, it is the perfect surgical tape for all your taping needs.



Latex sensitive reactions like these are eliminated.

Hy•Tape Latex Free is available in a variety of widths and package sizes.

The Original Pink Tape®
HY•TAPE®
INTERNATIONAL

P.O. Box 540, Patterson, NY 12563-0540
Toll-Free: 1-800-248-0101 Fax: 845-878-4104
Visit our website: www.hytape.com

NEW 3/4" SIZE AVAILABLE

Made in the U.S.A. Hy•Tape and "The Original Pink Tape" are registered trademarks of Hy•Tape International Inc.

Circle 110 on product information card

three treatment groups. It is concluded that single inhaler therapy with budesonide and formoterol is a clinically effective and well-tolerated treatment for patients with asthma that is not fully controlled by inhaled glucocorticosteroids alone.

A New Asthma Severity Index: A Predictor of Near-Fatal Asthma?—Lee P, Abisheganaden J, Chee CB, Wang YT. Eur Respir J 2001 Aug;18(2):272–278.

Bronchial hyperresponsiveness (BHR), measured as the provocative dose of inhaled histamine or methacholine required to produce a 20% fall in forced expiratory volume in one second (FEV_1) (PD20), is widely used as one of the indices of asthma severity. Excessive bronchoconstriction, reflected by the maximal percentage fall in forced vital capacity (FVC) at PD20 (ΔFVC %) during BHR testing, is considered to be the most important pathophysiological determinant in fatal asthma. The present study hypothesized that an index which combines both the ease of airway narrowing and excessive bronchoconstriction, ΔFVC %/log(PD20), may be better in assessing asthma severity, especially in those at risk of near-fatal attacks. The dose-response curves of 46 asthmatics who underwent methacholine challenge testing were studied. Group 1 (n=14) patients had mild disease, Group 2 (n=21) had moderate disease and Group 3 (n=11) had severe disease, as classified according to the Global Initiative for Asthma. Nine patients had prior intubation for near-fatal asthma. ΔFVC %/log (PD20) was better than ΔFVC % and PD20 in categorizing patients into the three severity groups ($p<0.0001$), but more importantly, it was able to discriminate patients with previous intubation from those without ($p=0.04$). It also correlated better with FEV_1 (% predicted), frequency of symptoms and inhaled steroid requirement than either index alone. It is concluded that the percentage fall in forced vital capacity/log of the provocative dose causing a 20% fall in forced expiratory volume in one second combines information on the ease and excessive degrees of airway narrowing in asthma. This new index may be better at assessing asthma severity and in discriminating those at risk of near-fatal attacks.

Exercise Tolerance in Children with Cystic Fibrosis Undergoing Lung Transplantation Assessment—Aurora P, Prasad SA, Balfour-Lynn IM, Slade G, Whitehead B, Dinwiddie R. Eur Respir J 2001 Aug;18(2):293–297.

The aim of this study was to compare the 6-min walk test against the recently developed 3-min step test, as measures of exercise tolerance in children with moderate to severe cystic fibrosis (CF) lung disease referred for lung transplantation assessment. Twenty-eight children with CF (16 girls, 12 boys), with a mean age of 13.7 yrs (range 7.2–17.8 yrs) and mean forced expiratory volume in one second of 34% predicted (range 17%–67%) were recruited. All subjects performed both the 6-min walk and 3-min step-tests. Outcome measures were maximum rise in heart rate (HR), and maximum fall in arterial oxygen saturation (S_{aO_2}). There was no significant difference in resting HR or S_{aO_2} prior to starting the two tests. Both step and walk tests produced significant rises in median HR (from 114–149 min^{-1}, $p<0.0005$, and 119–138 min^{-1}, $p<0.0005$, respectively) and significant falls in S_{aO_2} (both from 94–92%, $p<0.0005$). The step test produced a significantly greater percentage rise in HR (30% versus 18%, $p<0.0005$) and a significantly greater percentage fall in S_{aO_2} (4% versus 2%, $p=0.002$). Bland-Altman analysis gave wide 95% limits of agreement (10.7–29.3% for rise in HR, -2.14.6% for fall in S_{aO_2}). The step test was well tolerated. The 3-min step test produced a greater fall in S_{aO_2} and a greater rise in HR than the 6-min walk test in children with moderate to severe CF lung disease. It may be of value when assessing a child's suitability for lung transplantation.

Factors Associated with Poor Pulmonary Function: Cross-Sectional Analysis of Data from the ERCF, European Epidemiologic Registry of Cystic Fibrosis—Navarro J, Rainisio M, Harms HK, Hodson ME, Koch C, Mastella G, et al. Eur Respir J 2001 Aug;18(2):298–305.

The European Epidemiologic Registry of Cystic Fibrosis began collecting longitudinal data on European cystic fibrosis patients in 1994. A cross-sectional analysis was performed to identify the factors associated with low values of % predicted forced expiratory volume in one second (FEV_1) upon patient enrolment. Data from 7,010 patients aged ≥ yrs were included. Clinical conditions, microbiological isolates and medications reported at enrolment or within the following 180 days were analysed for age-specific associations. Factors associated with FEV_1 that were lower by >10% of pred values were: lower weight for age percentiles, haemoptysis, pneumothorax, pulmonary symptoms at presentation, *Pseudomonas aeruginosa*, *Burkholderia cepacia*, oral corticosteroids, nonsteroid anti-inflammatory drugs, dornase alfa, oxygen and assisted ventilation and, in patients >12 yrs old only, use of airway clearance techniques, inhaled bronchodilators, oral nutritional supplements, pancreatic enzymes and insulin or oral hypoglycaemics. Slightly impaired lung function (5–10%) was associated with: diabetes (≥ 18-yrs-old), gastro-oesophageal reflux, allergic bronchopulmonary aspergillosis, asthma-like symptoms, portal hypertension, *Aspergillus spp.* and *Candida spp.* Sex, *Haemophilus influenzae* and *Staphylococcus aureus* were not associated with impaired pulmonary status. Regular exercise (especially in older patients) and nasal polyposis were associated with slightly better FEV_1. The results confirm those of previous studies and suggest selective prescribing in sicker patients.

Influence of Neonatal Screening and Centralized Treatment on Long-Term Clinical Outcome and Survival of CF Patients—Merelle ME, Schouten JP, Gerritsen J, Dankert-Roelse JE. Eur Respir J 2001 Aug; 18(2):306–315.

After an experimental neonatal screening program for cystic fibrosis (CF) from 1973–1979, a follow-up study took place from 1980–1997. Patients were treated at specialized centres (C) or at local hospitals (non-C). Aims of the study were: 1) to determine whether the previously reported benefits from screening persisted with time and after adjustment for confounding variables; and 2) to investigate whether centre treatment was associated with improved prognosis of CF patients. Prognosis of patients detected by screening (S; n=24) was compared with patients detected clinically, born during (non-S; n=29) and after the screening programme (post-S; n=39). In addition, prognosis was compared between 45 C and 47 non-C patients. Multivariable regression analysis was used to compare survival and mixed-effects model regression analysis was used to compare clinical outcome between patients. The analyses included the variables screening, centre treatment, sex, meconium ileus and genotype. S patients had a significantly smaller decline in forced expiratory volume in one second (FEV_1) (difference +2.74% predicted) and significantly lower immunoglobulin-G (IgG) levels (difference -473.69 mg x dL^{-1}) than non-S patients until 12 yrs of age. At 12 yrs of age, vital capacity was significantly higher in S patients than in non-S patients (difference +362.79 mL). Survival seemed to be best for S patients compared to both non-S and post-S patients. Post-S patients were significantly heavier (difference in SD weight +0.77), had a significantly smaller decline in FEV_1 (difference +2.80% pred) and lower IgG levels (difference -453.04 mg x dL^{-1}) than non-S patients until 12 yrs of age. C patients had a significantly improved survival (relative risk (RR) 0.18, 95% confidence interval 0.05–0.57) than non-C patients. Early diagnosis through neonatal screening leads to better preservation of lung function in the long term in cystic fibrosis patients. Management of cystic fibrosis patients in specialized centres improves survival.

If it's Respiratory, it's from the AARC

ARDS: New Approaches to a Serious Respiratory Illness — An in-depth lecture about current knowledge and the latest treatments for this serious respiratory illness, ARDS. By Gordon R. Bernard, MD. 40-min. audiotape.
Item PAD827 $15.00 ($20.00 Nonmembers)

Does the "Machine" Make a Difference? — Reviews different ventilators and modalities available to respiratory therapists and their impact in clinical settings. By John J. Marini, MD. 40-min. audiotape.
Item PAD86 $15.00 ($20.00 Nonmembers)

How To Get Your "Dream Job" — Discusses what employers are looking for, finding jobs, networking to get noticed, sources of "insider" information, writing resumes and cover letters, interview skills, and salary negotiation. By Scott Reistad, RRT. 40-min. audiotape. **Item PAD829 $15.00 ($20.00 Nonmembers)**

Humidification Techniques: Efficiency and Costs — Describes all the options for providing humidity (heated humidifiers, heated wire circuits, HMEs, active HMEs) and reports on their performance and cost issues. By Richard D. Branson, BA, RRT, FAARC. 40-min. audiotape. **Item PAD8122 $15.00 ($20.00 Nonmembers)**

INO Therapy in Adult Respiratory Distress Syndrome — Presents advances in the use of INO in adult respiratory distress syndrome (ARDS) with a review of the latest findings in research, and future treatment of the syndrome. By Richard D. Branson, BA, RRT, FAARC. 40-min. audiotape.
Item PAD880 $15.00 ($20.00 Nonmembers)

INO Therapy in Neonatal and Pediatric Hypoxemia Respiratory Failure — Reviews advances in the use of INO in neonatal and pediatric respiratory failure along with the lastest finds in research. Describes future treatment for this illness. By John E. Thompson, RRT. 40-min. audiotape. **Item PAD879 $15.00 ($20.00 Nonmembers)**

NPPV in Acute and Long-Term Care — Addresses patient selection guidelines, NPPV initiation, clinical applications, ventilator and interface selections, modes of ventilation, weaning strategies, and complications and limitations. By Donna Wemhoff, BS, RRT, CPFT. 40-min. audiotape. **Item PAD866 $15.00 ($20.00 Nonmembers)**

Preparation for a Healthy Financial Future — A financial expert details how to manage personal finances and retirement planning. Presents information on how to get the most from your resources. By James Stevenson. 40-min. audiotape.
Item PAD863 $15.00 ($20.00 Nonmembers)

The "Facts" about Pressure Control Ventilation — Addresses the indications, clinical advantages, initiation, management, and monitoring of PCV. Focuses on patients benefiting from PCV and weaning strategies. By Donna Wemhoff, BS, RRT, CPFT. 40-min. audiotape. **Item PAD862 $15.00 ($20.00 Nonmembers)**

Transformation to Critical Thinking — Details strategy and tools necessary to assist staff in the improvement of their critical thinking skills. By Anna W. Parkman, MBA, RRT. 40-min. audiotape. **Item PAD820 $15.00 ($20.00 Nonmembers)**

Weaning in the ICU: Predictors and Strategies — Presents predictors and strategies that you may use to wean patients from mechanical ventilators in the critical care setting. By James K. Stoller, MD. 40-min. audiotape.
Item PAD8102 $15.00 ($20.00 Nonmembers)

Without Staff with Interpersonal Skills, You'll Never Have a Great Department —Explains the important skills to assist your staff in the improvement of their interpersonal abilities. Will help you take your department to the next level. By Scott Reistad, RRT. 40-min. audiotape. **Item PAD821 $15.00 ($20.00 Nonmembers)**

Call (972) 406-4663 with MasterCard, Visa, or Purchase Order or Fax to (972) 484-2720 / (972) 484-6010

SHIPPING AND HANDLING RATES — MUST BE INCLUDED ON ALL ORDERS

Order Total	Ground	AK,HI,PR
$15 or less	$4.25	$12.25
$15.01 to $25	$5.25	$14.50
$25.01 to $40	$6.25	$17.00
$40.01 to $60	$7.25	$19.25
$60.01 to $80	$8.25	$21.50

Order Total	Ground	AK,HI,PR
$80.01 to $100	$9.25	$25.00
$100.01 to $150	$10.25	$30.75
$150.01 to $200	$12.25	$33.00
$200.01 to $250	$14.25	$39.00

Order Total	Ground	AK,HI,PR
$250.01 to $300	$16.25	$44.00
$300.01 and up	$18.25	$58.50
$400 or more	$20.25	$64.50

Call for International Rates and Express Rates

Part II of Two Special Issues

Evidence-Based Medicine in Respiratory Care

Containing the papers and discussions from a Journal Conference presented under the auspices of the American Respiratory Care Foundation.

Supported by unrestricted educational grants from GlaxoSmithKline and Salter Labs.

Conference faculty members—front row, from left: Neil R MacIntyre MD FAARC, Dean R Hess PhD RRT FAARC, Maureen O Meade MD MSc, Shelley C Mishoe PhD RRT FAARC, Gordon H Guyatt MD MSc, Brian H Rowe MD MSc. Back row, from left: Gordon D Rubenfeld MD MSc, Robert L Chatburn RRT FAARC, A Gray Ellrodt MD, Charles G Durbin Jr MD FAARC, W Ward Flemons MD, Mark R Tonelli MD MA. Not pictured: William J Sibbald MD

CO-CHAIRS

Shelley C Mishoe PhD RRT FAARC
Dean R Hess PhD RRT FAARC

FACULTY

Robert L Chatburn RRT FAARC
Cleveland, Ohio
Charles G Durbin Jr MD FAARC
Charlottesville, Virginia
A Gray Ellrodt MD
Pittsfield, Massachusetts
W Ward Flemons MD
Calgary, Alberta, Canada
Gordon H Guyatt MD MSc
Hamilton, Ontario, Canada
Dean R Hess PhD RRT FAARC
Boston, Massachusetts
Neil R MacIntyre MD FAARC
Durham, North Carolina
Maureen O Meade MD MSc
Hamilton, Ontario, Canada
Shelley C Mishoe PhD RRT FAARC
Augusta, Georgia
Brian H Rowe MD MSc
Edmonton, Alberta, Canada
Gordon D Rubenfeld MD MSc
Seattle, Washington
William J Sibbald MD
Toronto, Ontario, Canada
Mark R Tonelli MD MA
Seattle, Washington

An Evidence-Based Approach to Acute Respiratory Distress Syndrome

Maureen O Meade MD MSc and Margaret S Herridge MD MSc

Introduction
Methods
Review of the Literature
Lung-Protective Ventilation Strategies
Inhaled Nitric Oxide
Prone Positioning
Late-Phase Corticosteroids
Surviving Acute Respiratory Distress Syndrome: Long-Term Follow-Up
Summary

We provide an evidence-based approach to managing patients with acute lung injury and acute respiratory distress syndrome (ARDS). We searched MEDLINE and the Cumulative Index to Nursing and Allied Health for randomized trials evaluating lung-protective ventilation strategies, inhaled nitric oxide, prone positioning, and late-phase corticosteroids for managing these patients, and for additional literature related to long-term follow-up of ARDS survivors. The results of our review suggest that pressure- and volume-limited ventilation, according to the ARDS Network protocol, can reduce mortality for patients with acute lung injury, and so may an "open lung" approach to mechanical ventilation. Those 2 strategies are currently being compared in 2 multicenter randomized trials. Although both inhaled nitric oxide therapy and prone positioning can produce dramatic acute improvements in oxygenation for some patients, there is no evidence that these interventions can benefit patients with respect to patient-important outcomes. Therefore it is unreasonable to be dogmatic about the role of inhaled nitric oxide and prone positioning in ARDS. The role of corticosteroids in the late phase of ARDS is unclear and remains a very important unanswered question. With respect to long-term follow-up, we found that pulmonary dysfunction is probably not a major source of morbidity for ARDS survivors, whereas neuropsychological dysfunction is prominent. Ongoing research may suggest interventions to improve the outcome of ARDS and of critical illness in general. *Key words: acute respiratory distress syndrome, ARDS, acute lung injury, ALI, critical care, mechanical ventilation.* [Respir Care 2001;46(12):1368–1376]

Introduction

The care of patients with acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) presents an interesting challenge to critical care clinicians, now more than ever before. The results of recent randomized clinical trials provide exciting evidence that our bedside deliberations over ventilation strategies may indeed influence survival. Leaders in pulmonary physiology and critical care are advocating tracheal gas insufflation and new strategies for patient positioning, while others are attempting to per-

Maureen O Meade MD MSc is affiliated with the Department of Medicine and the Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ontario, Canada, and with the Canadian Institutes of Health Research. Margaret S Herridge MD MSc is affiliated with the Department of Medicine, University of Toronto, Toronto, Ontario, Canada.

A version of this report was presented by Maureen O Meade MD MSc at the RESPIRATORY CARE Journal Conference, Evidence-Based Medicine in Respiratory Care, April 20–22, 2001, Banff, Alberta, Canada.

Correspondence: Maureen O Meade MD MSc, Department of Clinical Epidemiology and Biostatistics, HSC-2C10, McMaster University Health Sciences Centre, 1200 Main Street West, Hamilton ON L8N 3Z5, Canada. E-mail: meadema@hhsc.ca.

suade us to return to an age-old method of applying high levels of positive end-expiratory pressure (PEEP). Meanwhile, industry presents us with sophisticated technologies, novel therapies, and attractive liquids, all shown to acutely improve oxygenation. There are innumerable options.

Clinicians at the bedside often engage in discussions about the appropriateness of any or many of these strategies for individual ALI patients, referring to physiology, clinical research, laboratory research, and clinical experience. Our decisions for patient care often vary. Is there a standard way in which we should approach the available evidence?

One of the guiding tenets of evidence-based medicine is a hierarchy of evidence.[1] Evidence may derive from clinical observations, physiology and physiologic rationale, laboratory research, clinical research, randomized clinical trials, or systematic reviews. All of these types of evidence have an important role in clinical medicine, and all of them have limitations (Table 1).

An awareness and understanding of the hierarchy of evidence outlined in Table 1 can guide our decision-making. First, when considering a particular intervention for a patient with ALI, clinicians should strive to know the highest level of relevant evidence supporting (or refuting) an intervention. If the highest level of evidence is quite definitive (eg, a large randomized trial demonstrating a treatment effect that is both clinically important and statistically significant), there may be no need to consider lower levels of evidence. In ALI this is rarely the case and we must look further. If the highest level of evidence is relatively low in the hierarchy, one may consider other types of evidence. If the highest level of evidence is derived from a poorly designed study, that evidence should not necessarily supersede lower levels of evidence in the hierarchy. Even if results of multiple, well-designed, large, randomized trials support a particular intervention for populations of ALI patients, that evidence does not dictate our decisions, which must, ultimately, be patient-centered. This principle is illustrated in the following 2 examples.

First, there is clear evidence from several randomized trials and systematic reviews that aspirin prevents mortality in the setting of acute myocardial infarction.[2] However, no one would dispute a decision to withhold aspirin from an allergic patient who has suffered severe asthma attacks following prior aspirin ingestions. Second, there is strong evidence from a large randomized trial that a low tidal volume (V_T)/low airway pressure strategy improves survival for most ALI patients.[3] According to the study protocol, acidosis should not prompt a violation of the limits of airway pressure and V_T unless pH falls below 7.15. However, for a patient with ALI and a history of malignant arrhythmias, including cardiac arrest, who is awaiting placement of an automatic implantable defibrillator, it would be reasonable to keep pH $>$ 7.25 if that appears to be a threshold for premature ventricular contractions for that patient.

Table 1. Hierarchy of Evidence

Evidence Type	Limitations
n of 1 randomized trial	Results apply to a single patient only
Meta-analysis	Limited by the quality of included studies
Randomized controlled trial	Results address populations, not always individuals
Observational controlled study	Always prone to multiple sources of bias
Laboratory investigation	Uncertain generalizability to humans
Clinical observation	Unsystematic; extremely open to bias
Physiologic rationale	Frequently erroneous

There is often a great temptation to let clinical experience and physiologic rationale guide clinical decision-making, even when these conflict with the results of high-quality clinical research evidence. This approach can be potentially harmful to patients. In the 2 examples described above, clinical observations and physiologic rationale appropriately supersede recommendations that are based on a large and well-conducted randomized clinical trial. What if the patient with acute myocardial infarction had simply stated, "I am allergic to aspirin"? No doubt, caregivers would push the point and determine the nature of symptoms experienced with prior aspirin ingestion. If the patient had experienced episodes of dyspepsia, without gastrointestinal bleeding, rash, or bronchospasm, caregivers would be correct to recommend aspirin, explaining this recommendation to the patient. Similarly, if the patient with ALI did not have a history of malignant arrhythmias, then violating the study protocol would not be warranted unless that is how premature ventricular contractions were treated in the context of the clinical trial. Though pressure and volume limitation has been shown to save lives, preventing premature ventricular contractions through alterations in acid-base status has not. Therefore we must be extremely cautious in exercising our understanding of physiology if these actions counter an alternative course suggested by much higher levels of evidence.

This introduction describes an evidence-based approach to the management of ALI and ARDS patients. The following section outlines our review methods. Subsequently, we present the results of our review, and in the final section we discuss the implications for respiratory care.

Methods

This systematic review was conducted for the purposes of a presentation at the Respiratory Care Journal Conference in Banff, Alberta, in April 20–22, 2001. We were charged with the tasks of addressing questions of both (1) therapeutic efficacy and (2) long-term follow-up of ARDS

survivors. One person conducted the literature searches, one reviewed the titles and abstracts for potentially relevant articles, one reviewed all potentially relevant articles, and one selected articles for inclusion in this review, as described below.

To address questions of therapeutic efficacy, we searched MEDLINE (1966 to 2000) using the search terms "respiratory distress syndrome, acute," "human," and "randomized controlled trials." We also used the Cumulative Index to Nursing and Allied Health (1982 to 2000) and the Cochrane Database of Systematic Reviews. Our criteria for inclusion included:

Populations: critically ill adults with ALI or ARDS,

Interventions: pressure- and volume-limited ventilation strategies, high-PEEP strategies, prone ventilation, inhaled nitric oxide, and systemic corticosteroids for late-phase ARDS,

Control interventions: conventional care, and

Outcomes: mortality.

To address questions related to the long-term follow-up of ARDS patients we searched MEDLINE (1966 to 2000) using the search terms "respiratory distress syndrome," "human," and "follow-up studies OR cohort studies OR pulmonary function." We also used the Cumulative Index to Nursing and Allied Health (1982 to 2000) and the Cochrane Database of Systematic Reviews. We elected to review all studies of long-term follow-up in adult survivors of ARDS, excluding studies evaluating only long-term mortality, studies reporting on < 5 patients, and studies published exclusively in languages other than English.

We reviewed each article using an approach outlined in 2 articles from the *Users' Guide to the Medical Literature* series: "How to Appraise an Article about a Therapy or Prevention"[4] and "How to Appraise an Article about Prognosis."[5] To appraise articles about therapy, we looked for true randomization, concealment, blinding, baseline similarity of study groups, report of the use of co-interventions, rates of follow-up, and intention-to-treat analysis. To appraise articles on long-term follow-up we looked for the inclusion of a representative sample (high rates of follow-up) and unbiased outcome criteria.

We pooled data quantitatively only when it seemed appropriate based on examination of the populations, interventions, and control interventions in the original studies, based on visual inspection of study results, and based on formal tests for heterogeneity among study results.[6]

Review of the Literature

Lung-Protective Ventilation Strategies

Ventilator-associated lung injury can be caused by selective over-distention of relatively normal lung units (volutrauma),[7] repetitive opening and closing of terminal lung units (shearing injury),[8] oxygen toxicity,[9] and adverse effects of inflammatory mediators and oxidant molecules (biotrauma).[10] The most widely studied lung-protective strategies include pressure- and volume-limited ventilation strategies and "open lung" ventilation.

Pressure- and Volume-Limited Ventilation. There are 4 reported randomized trials of pressure- and volume-limited ventilation strategies, which have been conducted in Canada,[11] Europe,[12] Maryland,[13] and across the United States.[3] A fifth study compared pressure-limited and volume-controlled modes, but that study did not compare ventilation strategies with alternative constraints of pressure and volume, or PEEP, so we excluded that study.[14]

All 4 studies included ARDS patients, and both the ARDS Network study[3] and the Canadian trial included patients with less severe ALI. The European trial was unique in the inclusion of patients with single organ failure (lung injury), only. The pressure- and volume-limited ventilation strategies included V_T of 4–8 mL/kg in most studies, and as high as 6–10 mL/kg in the European trial. Limits of airway pressures ranged from 25 to 30 cm H_2O, and some studies focused on plateau airway pressure[3,12,13] whereas others focused on peak inspiratory airway pressure.[11] Control group strategies limited V_T to the traditional range of 10–15 mL/kg (simply 12 mL/kg in the ARDS Network trial), and airway pressures in control groups ranged from 45 to 60 cm H_2O. The studies differed with respect to the management of acidosis. ARDS Network investigators were most aggressive, endeavoring to keep pH > 7.30 for all patients, and allowing violations of the V_T and airway pressure limits when pH fell below 7.15. In contrast, the Canadian investigators strove to keep pH > 7.35 but did not dictate volume and pressure violations until pH fell to 7.00.

The ARDS Network investigators were among the most scrupulous about controlling important threats to the validity of their results. All studies were randomized and concealed, and all four found similarity of the 2 study groups at the time of randomization with respect to important determinants of outcome. Unbalanced use of co-interventions (for instance, inhaled nitric oxide) between study groups did not appear to be an important feature of any of the studies. All of the studies included complete follow-up and intention-to-treat analysis. The ARDS Network study was one of three that were stopped early according to a priori stopping rules.[3,12,13]

The study results are outlined in Table 2. Only the ARDS Network trial found a significantly lower mortality in association with the experimental strategy. The relative risk of mortality associated with low-V_T ventilation was 0.78 (95% confidence interval 0.65–0.93). This means that for every 12 study patients ventilated using the pressure- and volume-limited approach, one death was prevented at the

28th day of study. The differences among the study results must be considered in the context of the similarities and differences among the studies discussed above. More importantly, the conflicting results should be considered in light of the finding that the differences in airway pressures and in V_T between experimental and control groups in the ARDS Network trial were greater than in any other trial. Only in the ARDS Network trial did the plateau airway pressure difference between groups cross the physiologically important threshold of 30 cm H_2O, a threshold beyond which over-distention injury is believed most likely to occur.[15] For that reason and the differences in the management of acidosis among the trials, we do not believe it is reasonable to pool data across these 4 studies in a quantitative meta-analysis.

"Open Lung" Ventilation. An "open lung" approach to mechanical ventilation was evaluated in a randomized controlled trial conducted by Amato et al.[16] Patients in the "open lung" group were ventilated using pressure control mode, targeting V_T to 6 mL/kg, and restricting plateau airway pressures to $\leq$ 40 cm H_2O. High levels of PEEP were used in that group, as determined by static pressure-volume curves, conducted at the time of randomization, that were used to identify a lower inflection point, and PEEP was applied at 2 cm H_2O above that point until the concentration of inspired oxygen had been titrated to < 0.4. Finally, in that group, lung recruitment maneuvers were conducted following each disconnect of the patient from the ventilator, in order to recruit alveoli that may have collapsed during the disconnect. The lung recruitment maneuver consisted of a sustained inflation at 35–40 cm H_2O for 40 seconds. In contrast, patients in the control group were ventilated using volume-cycled modes, at a V_T of 12 mL/kg. There were no limits on plateau airway pressure in the control group, and investigators followed a more conventional strategy for titrating PEEP, which resulted in a significant PEEP difference between the 2 study groups. This study was also stopped early. Investigators observed a quicker recovery of lung function associated with the "open lung" approach and, more importantly, a large and statistically significant reduction in the risk of mortality (71% for controls versus 38% for the experimental group, 95% confidence interval 0.31–0.91).

Table 2. Results of Studies of Pressure- and Volume-Limited Ventilation

First Author	*n*	Control Mortality (%)	PVLV Mortality (%)	RR (95% CI)
Stewart[11]	120	46.7	50.0	1.07 (0.74–1.55)
Brochard[12]	116	37.9	46.6	1.23 (0.80–1.89)
Brower[13]	52	46.0	50.0	1.09 (0.62–1.91)
ARDS Network[3]	861	39.8	31.0	0.78 (0.65–0.93)

PVLV = pressure- and volume-limited ventilation
RR = relative risk of mortality
CI = confidence interval
ARDS = acute respiratory distress syndrome

Inhaled Nitric Oxide

Inhaled nitric oxide is a selective pulmonary vasodilator that can improve ventilation and perfusion matching to achieve a dramatic acute improvement in oxygenation for some patients. However, the potential for harm and the costs of inhaled nitric oxide therapy are substantial.

The question of whether inhaled nitric oxide can improve patient-important outcomes has been evaluated in a number of trials conducted in adult intensive care units (ICUs) across America[17] and Europe,[18] and in Salt Lake City[19] and Montreal.[20] Most studies focused on ARDS patients, though the European study included ALI patients, and one of the single-center studies included children. Only one study was blinded.[17] Table 3 illustrates the results of those trials. Our assessment of the similarities and differences of those studies, and our visual assessment of the estimates of efficacy with respect to patient mortality across studies, lead us to conduct a formal statistical test of heterogeneity and, ultimately, to pool the results across studies for the purpose of the present review. No study found an important survival benefit and (using either a random effects model or a fixed effects model) the pooled estimate of the relative risk of mortality is 1.12, with a 95% confidence interval that overlaps 1.0 (0.90–1.40). In other words, the best estimate of relative risk indicates that mortality is 12% higher for patients who receive inhaled nitric oxide therapy than for patients who do not. However, the results do not exclude the potential for a 10% improvement in survival, based on the lower level of the confidence interval at 0.90. These results are consistent with the findings of a recent Cochrane review.[21]

Prone Positioning

The mechanisms of potential benefit with prone positioning have been studied extensively and include:

Table 3. Results of Studies of Inhaled Nitric Oxide Therapy

First Author	*n*	Control Mortality (%)	Nitric Oxide Mortality (%)	RR (95% CI)
Dellinger[17]	177	29.8	29.2	0.97 (0.60–1.57)
Lundin[18]	180	43.7	51.6	1.17 (0.86–1.59)
Michael[19]	40	45.0	55.0	1.21 (0.66–2.23)
Troncy[20]	30	53.3	60.0	1.12 (0.61–2.06)

RR = relative risk of mortality
CI = confidence interval

• A reduction in the compressive forces of the heart on dorsal lung regions,

• Re-expansion of lung regions suffering gravity-induced atelectasis,

• Improvement in chest wall compliance and a resultant increase in functional residual capacity, with an attendant (hypothetical) reduction in ventilator-associated lung injury,

• Little effect on regional perfusion, with a resultant improvement in the matching of ventilation and perfusion, and,

• Superior draining of bronchial secretions.

Systematic observations of the physiologic effects of prone positioning are reported in 14 case series, including 260 ARDS patients, of which 69% responded with an acute improvement in oxygenation.[22–35] The reproducibility of that response was variable.[25,26,35] Patients among those studies were cared for in the prone position for periods ranging from 2 to 20 hours. The duration of effect also differed across studies. Six of the studies took a systematic look at adverse effects,[23,24,26,27,30,33] which were rare but included extubation, central line removal, central line compression, supraventricular tachycardia, acute apical atelectasis, acute deterioration in oxygenation, and hip and shoulder contractures. In addition, clinicians familiar with prone ventilation can attest to the pressure necrosis and severe edema that can occur on the face. They are also concerned about delayed resuscitation from cardiac arrest for patients who are nursed in the prone position and must be turned supine while taking care of all central venous lines, chest tubes, and the endotracheal tube, in the event of a cardiac arrest.

There is currently one completed trial and there are 2 ongoing randomized trials of prone positioning for ARDS patients.[36] Gattinoni et al enrolled approximately 300 ARDS patients from across Europe in a randomized trial in which the experimental group was ventilated in the prone position for 6 hours daily and the control group received usual care without prone-position ventilation.[36] The study was not concealed, but patients were shown to be similar in the 2 groups at baseline with respect to known determinants of outcome, there were only minimal crossovers or uses of co-interventions, and there was 100% follow-up, and an intention-to-treat analysis. There was no difference between the groups with respect to the duration of mechanical ventilation or patient mortality. In one of the 2 ongoing European randomized trials, patients with a ratio of arterial partial pressure of oxygen to fraction of inspired oxygen (P_{aO_2}/F_{IO_2}) $\leq$ 300 were randomly assigned to either prone positioning for at least 8 hours daily or supine positioning.[37] Severely hypoxic patients (P_{aO_2}/F_{IO} $\leq$ 60 while on 100% oxygen) were able to cross over to receive prone ventilation. A midpoint interim analysis including 384 patients has revealed baseline similarity between the 2 study groups and no apparent difference in mortality.[38]

Late-Phase Corticosteroids

Meduri et al randomly assigned patients with severe ARDS unresolving at 7 days and no evidence of untreated infection to receive either methylprednisolone (at 2 mg/kg/d for 32 days) or a placebo control.[39] Patients in both groups underwent high surveillance for new infections. This study had a number of strengths, including concealed randomization and blinding of patients, caregivers, investigators, and outcome assessors. The statistical approaches may, however, produce misleading results. Patients were randomly assigned to the 2 groups at a rate of 2 to 1, so that there were half as many patients randomized to the control group. In addition, one half of control patients crossed over at day 10. As a result of unconventional stopping rules, the study ended after the enrollment of 24 patients and, as a result of the other statistical issues described above, only 4 patients received only placebo therapy. In general, the allowance of crossovers in a randomized trial will lead to an underestimation of treatment effects. However, in the context of such a small study, with one-sided statistical tests and unconventional stopping rules, it is possible that the observed results are a chance phenomenon. Having said that, study results were consistent with a potentially important benefit from corticosteroids in late-phase ARDS. At day 10, patients in the steroid group were progressing significantly better with respect to severity of lung injury (as measured by Lung Injury Score and P_{aO_2}/F_{IO_2}), organ dysfunction (as measured by the Multiple-Organ Dysfunction Score), extubation rates, and survival rates. Crossovers were allowed at that time, and 4 placebo patients crossed over. Three of those 4 patients died. Conducting an intention-to-treat analysis, there were zero ICU deaths in the steroid group, compared to 5 in the placebo group ($p = 0.032$), and there were 2 and 5 hospital deaths, respectively ($p = 0.26$).

Surviving Acute Respiratory Distress Syndrome: Long-Term Follow-Up

ARDS follow-up studies have evolved from isolated pulmonary function assessments to pulmonary function assessments combined with functional outcome measures and generic and disease-specific quality of life measures. This evolution of the ARDS outcomes literature reflects the realization that multiple morbid outcomes need to be measured simultaneously to understand the nature and determinants of functional disability and how this can be remediated. Other limitations of the current literature include (1) the difficulty in retaining the follow-up population over time, (2) the population heterogeneity inherent in

the ARDS definition, and (3) the need for a comprehensive ICU and post-ICU data set to understand the impact of ICU and post-ICU intervention on morbidity. As well, many researchers appreciate the need for in-person dialogue with ARDS survivors to understand concerns and complaints that may not be captured by structured quality-of-life questionnaires. Ambulatory follow-up with a home visit program may help to overcome many of those obstacles and may represent a viable new model for ARDS outcomes research.

Pulmonary Function. Pulmonary function has been evaluated in 18 studies of 392 ARDS survivors included in this review.[40–57] The rates of follow-up of survivors differed among the studies, introducing a potential threat of selection bias. If patients do not follow up because they are too debilitated, reports may be over-optimistic as a result. If investigators focus their research on symptomatic patients, the reports may overestimate the degree of pulmonary dysfunction in ARDS survivors. The degree of follow-up and the reasons for lack of follow-up in many of the studies were not explicit. Six groups of investigators attempted serial follow-up of ARDS survivors.[44,45,48,50,52,53] Seven groups reported essentially normal pulmonary function beyond 6 months to 2 years, aside from persistently decreased measures of diffusion capacity.[42,43,46,50,51,54,57] Five reported minimal to mild abnormalities of pulmonary function in up to 25–50% of patients at that time.[41,45,47,49,51] Two studies reported moderate to severe abnormalities in a total of 6 patients at 1 year or beyond.[44,45] In other words, the rate of important abnormalities in pulmonary function test (PFT) results is not high in ARDS survivors. The severity of abnormalities was not documented in 3 studies.[53,55,56] Pulmonary function abnormalities included a broad range of obstructive and restrictive patterns, the latter being somewhat more prominent. A persistent reduction in diffusion capacity was very common, with or without other associated abnormalities. Interestingly, among the 10 studies that reported on patient symptoms,[40–45,50,52,53,55] only five observed any degree of pulmonary symptoms.[44,50,52,53,55] Three studies found that pulmonary function abnormalities were directly related to the severity of ARDS,[43,52,56] and two did not.[53,57] Two studies found that the degree of abnormalities in PFT results were related to the duration of ARDS,[43,53] and two did not.[47,57]

The heterogeneity in reported pulmonary function is somewhat puzzling. A recent follow-up study of ambulatory patients may provide important insights into those apparently discordant findings.[45] A proportion of patients with bronchiolitis obliterans and bronchiolitis obliterans with organizing pneumonia were captured by the American European Consensus Conference definition for ARDS.[58] The natural pulmonary history of these diseases is very different from diffuse alveolar damage and if left untreated will progress to pulmonary fibrosis and substantial restrictive pulmonary disease. The heterogeneity of the ARDS population may directly impact the degree of reported pulmonary morbidity and may account for the differences.

Functional Exercise Capacity. Two of the studies reported above evaluated functional exercise capacity, using a 6-minute walk test either between 1 and 2 years after ARDS[41] or during a longitudinal follow-up at 1, 6, and 12 months.[45] In both studies, functional capacity was moderately limited, but not as a result of respiratory problems, as evidenced by the essentially normal PFT results. Furthermore, in a study of ambulatory patients, with 90% follow-up of all registered ARDS survivors,[45] only 1% of the patients were observed to desaturate to $< 88\%$ during exercise at 1 year. Clinical examination suggested that poor functional capacity was related to generalized muscle weakness, muscle wasting, ICU-acquired nerve entrapment syndromes, and heterotopic ossification. Consistent with this hypothesis, improvements in exercise capacity over the first year mirrored global recovery.[45]

Health-Related Quality of Life. All 8 investigations of health-related quality of life (HRQL) among ARDS survivors employed generic scores and observed significant impairment, primarily in the domain of physical function.[41,45,52,59–63] Three studies also used respiratory-disease-specific questionnaires and found that impaired function was consistent with the presence of moderately severe respiratory disease.[41,52,60] One set of investigators suggested that respiratory dysfunction in ARDS survivors may therefore have been previously underestimated.[60] However, in studies that conducted concurrent PFTs and tests of functional exercise capacity, results from those tests were relatively normal, suggesting that impaired physical function in ARDS survivors is unlikely to be related to pulmonary disease.[41,45] Patients do report exertional dyspnea but characterize it as extrapulmonary dyspnea on the basis of a perceived increased work of breathing related to global muscle loss/weakness.[45] These findings highlight the difficulty in applying a disease-specific HRQL measure to patients for whom the instrument was not validated: results may be misleading. An alternative hypothesis for the Davidson et al results[60] relates to heterogeneity in the population of patients captured by the ARDS definition. If those investigators captured a greater proportion of patients with bronchiolitis obliterans/bronchiolitis obliterans with organizing pneumonia in their cohort, they may have reported an increased incidence of true pulmonary morbidity.

Neuropsychological Morbidity. Four groups have investigated a number of neuropsychological sequelae of

ARDS in survivors and have observed substantial cognitive and affective impairment at hospital discharge, with cognitive impairment persisting after 1 year,[63] post-traumatic stress disorder,[45,61] with greater recall of traumatic ICU events correlating with worse neuropsychological complaints and HRQL,[62] and prominent hallucinations, paranoia, depressed mood, and personality changes.[45,61]

A prospective study of ambulatory ARDS survivors is currently underway in Toronto.[45] ARDS patients are registered prospectively and followed in an ambulatory setting or in their homes at 1, 6, and 12 months, and every 6 months thereafter to 5 years after discharge from ICU. Each patient undergoes a structured and unstructured interview, limited physical examination, PFT, 6-minute walk test, HRQL assessment with the Medical Outcomes Study Short Form 36 and the St George's Respiratory Questionnaire, and detailed evaluation of his or her pattern and cost of health care utilization. The study is the most comprehensive assessment of ARDS survivors to date. Results are likely to resolve uncertainty about the prominence of pulmonary morbidity in ARDS survivors, will help explain the evolution of morbidities over time, and may direct ICU interventions to improve the outcome of ARDS (or research in that field) and of critical illness in general.

Summary

The results of randomized trials of lung-protective ventilation strategies have provided exciting evidence that decisions about ventilator strategies can have an important effect on the outcome of critical illness. Pressure- and volume-limited ventilation using the ARDS Network protocol can reduce mortality for ALI patients, and Amato's "open lung" approach may also reduce mortality.

Currently the most intensely pursued clinical research question for ALI and lung-protective ventilation is whether a ventilation strategy that combines pressure and volume limitation with additional maneuvers to "open" the lung are superior to pressure and volume limitation alone, with respect to improving mortality among critically ill ALI patients. This question is currently under investigation in 2 independent multicenter randomized trials underway in the United States and Canada.

A discussion of lung-protective ventilation would not be complete without mention of additional adjunctive strategies that remain investigational. Partial liquid ventilation and aerosolized surfactant therapy are currently under investigation in adult ICUs. Their roles remain to be determined. Extracorporeal membrane oxygenation is currently in use in some centers, though 2 randomized trials (one in the 1970s and one in the 1990s) found no improvement in the probability of long-term survival, in spite of the ability to support gas exchange.[64,65] High-frequency oscillation and tracheal gas insufflation are relatively new strategies in adult ICUs and may have an important role in managing adult ALI, though they have yet to be evaluated in the context of randomized trials.

Although inhaled nitric oxide therapy can produce dramatic acute improvement in oxygenation in some patients, there is no evidence that it can benefit patients with respect to patient-important outcomes, even for subgroups of patients in respiratory *extremis*. Inhaled nitric oxide should be limited to salvage therapy of patients in respiratory *extremis* only, and ideally in the context of further systematic study.

Prone positioning, though it makes good sense physiologically and has been shown to effect acute improvement in oxygenation for some patients, has a number of associated practical deterrents. Moreover, one randomized trial found no evidence of benefit with respect to patient-important outcomes. Pending publication of current studies, it is unreasonable to be dogmatic about the role of prone positioning in ARDS patients. If results of current studies are as presented above, practical issues provide ample reason not to use prone positioning. Clinicians may argue that they are inclined to prone positioning for longer periods with more frequent or less frequent changes to supine position and, therefore, that they will continue to use prone positioning ventilation avidly. We suggest that such clinicians consider systematically evaluating their experience with alternative prone positioning strategies in the context of clinical research.

The role of corticosteroids in late-phase ARDS is unclear and remains a very important question. The potential for harm, determined in studies of steroids for sepsis and early ARDS, warrants restricting late-phase steroids to research settings.

Finally, pulmonary dysfunction is probably not a major source of morbidity for ARDS survivors. Global functional disability may relate most to the profound muscle wasting and deconditioning associated with surviving an episode of critical illness. Neuropsychological dysfunction is prominent. Ongoing research may suggest interventions to improve the outcome of ARDS and of critical illness in general.

REFERENCES

1. Guyatt GH, Haynes RB, Jaeschke RZ, Cook DJ, Green L, Naylor CD, et al. Users' guides to the medical literature: XXV. Evidence-based medicine: principles for applying the users' guides to patient care. The Evidence Based Medicine Working Group. JAMA 2000; 284(10):1290–1296.
2. Catella-Lawson F, FitzGerald GA. Confusion in reperfusion: problems in the clinical development of antithrombotic drugs. Circulation 1997;95(4):793–795.
3. The Acute Respiratory Distress Syndrome Network. Ventilation with lower tidal volumes as compared with traditional tidal volumes for acute lung injury and the acute respiratory distress syndrome. N Engl J Med 2000;342(18):1301–1308.

4. Guyatt GH, Sackett DL, Cook DJ. Users' guides to the medical literature. II. How to use an article about therapy or prevention. A. Are the results of the study valid? The Evidence-Based Medicine Working Group. JAMA 1993;270(21):2598–2601.
5. Laupacis A, Wells G, Richardson WS, Tugwell P. Users' guides to the medical literature. V. How to use an article about prognosis. The Evidence Based Medicine Working Group. JAMA 1994;272(3):234–237.
6. Oxman AD, Cook DJ, Guyatt GH. Users' guides to the medical literature. VI. How to use an overview. The Evidence-Based Medicine Working Group. JAMA 1994;272(17):1367–1371.
7. Caldwell EJ, Powell RD, Mullooly JP. Interestitial emphysema: a study of physiologic factors involved in experimental induction of the lesion. Am Rev Respir Dis 1970;102(4):516–525.
8. Muscedere JG, Mullen BM, Gan K, Slutsky AS. Tidal ventilation at low airway pressures can augment lung injury. Am J Respir Crit Care Med 1994;149(5):1327–1334.
9. Bryan CL, Jenkinson SG. Oxygen toxicity. Clin Chest Med 1988; 9(1):141–152.
10. Ranieri VM, Suter PM, Tortorella C, De Tullio R, Dayer JM, Brienza A, et al. Effect of mechanical ventilation on inflammatory mediators in patients with acute respiratory distress syndrome: a randomized controlled trial. JAMA 1999;282(1):54–61.
11. Stewart TE, Meade MO, Cook DJ, Granton JT, Hodder RV, Lapinsky SE, et al. Evaluation of a ventilation strategy to prevent barotrauma in patients at high risk for acute respiratory distress syndrome. Pressure- and Volume-Limited Ventilation Strategy Group. N Engl J Med 1998;338(6):355–361.
12. Brochard L, Roudot-Thoraval F, Roupie E, Delclaux C, Chastre J, Fernandez-Mondejar E, et al. Tidal volume reduction for prevention of ventilator-induced lung injury in acute respiratory distress syndrome. The Multicenter Trail Group on Tidal Volume Reduction in ARDS. Am J Respir Crit Care Med 1998;158(6):1831–1838.
13. Brower RG, Shanholtz CB, Fessler HE, Shade DM, White P Jr, Wiener CM, et al. Prospective, randomized, controlled clinical trial comparing traditional versus reduced tidal volume ventilation in acute respiratory distress syndrome patients. Crit Care Med 1999;27(8): 1492–1498.
14. Rappaport SH, Shpiner R, Yoshihara G, Wright J, Chang P, Abraham E. Randomized, prospective trial of pressure-limited versus volume-controlled ventilation in severe respiratory failure. Crit Care Med 1994;22(1):22–32.
15. Slutsky AS. Mechanical ventilation. American College of Chest Physicians' consensus conference. Chest 1993;104(6):1833–1859.
16. Amato MB, Barbas CS, Medeiros DM, Magaldi RB, Schettino GP, Lorenzi-Filho G, et al. Effect of a protective-ventilation strategy on mortality in the acute respiratory distress syndrome. N Engl J Med 1998;338(6):347–354.
17. Dellinger RP, Zimmerman JL, Taylor RW, Straube RC, Hauser DL, Criner GJ, et al. Effects of inhaled nitric oxide in patients with acute respiratory distress syndrome: results of a randomized phase II trial. Inhaled Nitric Oxide in ARDS Study Group. Crit Care Med 1998; 26(1):15–23.
18. Lundin S, Mang H, Smithies M, Stenqvist O, Frostell C. Inhalation of nitric oxide in acute lung injury: results of a European multicentre study. The European Study Group of Inhaled Nitric Oxide. Intensive Care Med 1999;25(9):911–919.
19. Michael JR, Barton RG, Saffle JR, Mone M, Markewitz BA, Hillier K, et al. Inhaled nitric oxideversus conventional therapy: effect on oxygenation in ARDS. Am J Respir Crit Care Med 1998;157(5 Pt 1):1372–1380.
20. Troncy E, Collet JP, Shapiro S, Guimond JG, Blair L, Ducruet T, et al. Inhaled nitric oxide in acute respiratory distress syndrome: a pilot randomized controlled study. Am J Respir Crit Care Med 1998; 157(5 Pt 1):1483–1488.
21. Sokol J, Jacobs SE, Bohn D. Inhaled nitric oxide for acute hypoxemic respiratory failure in children and adults (Cochrane Review). In: The Cochrane Library, 3, 2001. Oxford: Update Software.
22. Douglas WW, Rehder K, Beynen FM, Sessler AD, Marsh HM. Improved oxygenation in patients with acute respiratory failure: the prone position. Am Rev Respir Dis 1977;115(4):559–566.
23. Langer M, Mascheroni D, Marcolin R, Gattinoni L. The prone position in ARDS patients. a clinical study. Chest 1988;94(1):103–107.
24. Stocker R, Neff T, Stein S, Ecknauer E, Trentz O, Russi E. Prone positioning and low- volume pressure-limited ventilation improve survival in patients with severe ARDS. Chest 1997;111(4):1008–1017.
25. Mure M, Martling CR, Lindahl SGE. Dramatic effect on oxygenation in patients with severe acute lung insufficiency treated in the prone position. Crit Care Med 1997;25(9):1539–1544.
26. Fridrich P, Krafft P, Hochleuthner H, Mauritz W. The effects of long-term prone positioning in patients with trauma-induced adult respiratory distress syndrome. Anesth Analg 1996;83(6):1206–1211.
27. Chatte G, Sab JM, Dubois JM, Sirodot M, Gaussorgues P, Robert D. Prone position in mechanically ventilated patients with severe acute respiratory failure. Am J Respir Crit Care Med 1997;155(2):473–478.
28. Pelosi P, Tubiolo D, Mascheroni D, Vicardi P, Crotti S, Valenza F, Gattinoni L. Effects of prone position on respiratory mechanics and gas exchange during acute lung injury. Am J Respir Crit Care Med 1998;157(2):387–393.
29. Pappert D, Rossaint R, Slama K, Gruning T, Falke KJ. Influence of positioning on ventilation-perfusion relationships in severe adult respiratory distress syndrome. Chest 1994;106(5):1511–1516.
30. Voggenreiter G, Neudeck F, Aufmkolk M, Fassbinder J, Hirche H, Obertacke U, Schmidt-Neuerburg KP. Intermittent prone positioning in the treatment of severe and moderate posttraumatic lung injury. Crit Care Med 1999;27(11):2375–2382.
31. Blanch L, Mancebo J, Perez M, Martinez M, Mas A, Bethese AJ, et al. Short-term effects of prone position in critically ill patients with acute respiratory distress syndrome. Intensive Care Med 1997;23(10): 1033–1039.
32. Brazzi L, Pelosi P, Gattinoni L. Prone position in mechanically ventilated patients. Monaldi Arch Chest Dis 1998;53(4):410–414.
33. Nakos G, Tsangaris I, Kostanti E, Lachana A, Koulouras V, Kastani D. Effect of prone position on patients with hydrostatic pulmonary edema compared with patients with acute respiratory distress syndrome and pulmonary fibrosis. Am J Respir Crit Care Med 2000; 161(2 Pt 1):360–368.
34. Vollman KM, Bander JJ. Improved oxygenation utilizing a prone positioner in patients with acute respiratory distress syndrome. Intensive Care Med 1996;22(10):1105–1111.
35. Jolliet P, Bulpa P, Chevrolet JC. Effects of the prone position on gas exchange and hemodynamics in severe acute respiratory distress syndrome. Crit Care Med 1998;26(12):1977–1985.
36. Gattinoni L, Tognoni G, Pesenti A, Taccone P, Mascheroni D, Labarta V, et al. Effect of prone positioning on the survival of patients with acute respiratory failure. N Engl J Med 2001;345(8):568–573.
37. Gaillard S, Guerin C, Ayzac L, Girard R, for the investigators of the prone position French trial. A multicenter randomized trial of prone position in acute respiratory failure (abstract). Am J Respir Crit Care Med 2000;161:A380.
38. Gaillard S, Guerin C, Ayzac L, Girard R, for the investigators of the prone position French trial. A multicenter randomized trial of prone position in acute respiratory failure: interim analysis (abstract). Am J Respir Crit Care Med 2001;1613:A16.
39. Meduri GU, Headley AS, Golden E, Carson SJ, Umberger RA, Kelso T, Tolley EA. Effect of prolonged methylprednisolone therapy in unresolving acute respiratory distress syndrome: a randomized controlled trial. JAMA 1998;280(2):159–165.

40. Aggarwal AN, Gupta D, Behera D, Jindal SK. Analysis of static pulmonary mechanics helps to identify functional defects in survivors of acute respiratory distress syndrome. Crit Care Med 2000; 28(10):3480–3485.
41. Cooper AB, Ferguson ND, Hanly PJ, Meade MO, Kachura JR, Granton JT, Slutsky AS, Stewart TE. Long-term follow-up of survivors of acute lung injury: lack of effect of a ventilation strategy to prevent barotrauma. Crit Care Med 1999;27(12):2616–2621.
42. Douglas ME, Downs JB. Pulmonary function following severe acute respiratory failure and high levels of positive end-expiratory pressure. Chest 1977;71(1):18–23.
43. Elliott CG, Morris AH, Cengiz M. Pulmonary function and exercise gas exchange in survivors of adult respiratory distress syndrome. Am Rev Respir Dis 1981;123(5):492–495.
44. Ghio AJ, Elliott CG, Crapo RO, Berlin SL, Jensen RL. Impairment after adult respiratory distress syndrome. Am Rev Respir Dis 1989; 139(5):1158–1162.
45. Herridge MS, Cheung AM, Tansey CM, Matte-Martyn A, Cooper A, Guest C, et al, and the Canadian Critical Care Trials Group. Long term outcomes in survivors of ARDS (abstract). Am J Respir Crit Care Med 2001;163:A253.
46. Kauffmann GW, Vogel W, Ruhle KH, Friedberg HH, Papacharalampous X. [Monitoring studies of survivors of shock lung (ARDS): correlation of radiology and lung function.] ROFO Fortschr Geb Rontgenstr Nuklearmed 1983;138(3):292–296. *article in German*
47. Klein JJ, van Haeringen JR, Sluiter HJ, Holloway R, Peset R. Pulmonary function after recovery from the adult respiratory distress sydrome. Chest 1976;69(3):350–355.
48. Knoch M, Kukule I, Muller E, Holtermann W. [Pulmonary function one year after extracorporeal lung assist: a long-term follow-up of patients with acute adult respiratory distress syndrome.] Anasthesiologie Intensivmed Notfallmed Schmerzther 1992;27(8):477–482. *article in German*
49. Krieger HG, Tauchert S, Heinrich D, Kramer W, Knorpp K, Lasch HG. [Pulmonary function parameters of shock lung patients: results of a follow-up study.] Pneumologie 1990;44 Suppl 1:318–319. *article in German*
50. Lakshminarayan S, Stanford RE, Petty TL. Prognosis after recovery from adult respiratory distress syndrome. Am Rev Respir Dis 1976; 113(1):7–16.
51. Luhr O, Aardal S, Nathorst-Westfelt U, Berggren L, Johansson LA, Wahlin L, Frostell C. Pulmonary function in adult survivors of severe acute lung injury treated with inhaled nitric oxide. Acta Anaesthesiol Scand 1998;42(4):391–398.
52. McHugh LG, Milberg JA, Whitcomb ME, Schoene RB, Maunder RJ, Hudson LD. Recovery of lung function in survivors of the acute respiratory distress syndrome. Am J Respir Crit Care Med 1994;150(1): 90–94.
53. Peters JI, Bell RC, Prihoda TJ, Harris G, Andrews C, Johanson WG. Clinical determinants of abnormalities in pulmonary function in survivors of the adult respiratory distress syndrome. Am Rev Respir Dis 1989;139(5):1163–1168.
54. Rotman HH, Lavelle TF Jr, Dimcheff DG, VandenBelt RJ, Weg JG. Long-term physiologic consequences of the adult respiratory distress syndrome. Chest 1977;72(2):190–192.
55. Simpson DL, Goodman M, Spector SL, Petty TL. Long-term follow-up and bronchial reactivity testing in survivors of the adult respiratory distress syndrome. Am Rev Respir Dis 1978;117(3):449–454.
56. Suchyta MR, Elliott CG, Jensen RL, Crapo RO. Predicting the presence of pulmonary function impairment in adult respiratory distress syndrome survivors. Respiration 1993;60(2):103–108.
57. Yahav J, Lieberman P, Molho M. Pulmonary function following the adult respiratory distress syndrome. Chest 1978;74(3):247–250.
58. Bernard GR, Artigas A, Brigham KL, Carlet J, Falke K, Hudson L, et al. The American-European Consensus Conference on ARDS. Definitions, mechanisms, relevant outcomes, and clinical trial coordination. Am J Respir Crit Care Med 1994;149(3 Pt 1):818–824.
59. Chaboyer W. Survivors of acute respiratory distress syndrome may experience lower quality of life than other populations. Aust Crit Care 1999;12(3):119.
60. Davidson TA, Caldwell ES, Curtis JR, Hudson LD, Steinberg KP. Reduced quality of life in survivors of acute respiratory distress syndrome compared with critically ill control patients. JAMA 1999; 281(4):354–360.
61. Wienert CR, Gross CR, Kangas JR, Bury CL, Marinelli WA. Health-related quality of life after acute lung injury. Am J Respir Crit Care Med 1997;156(4 Pt 1):1120–1128.
62. Schelling G, Stoll C, Haller M, Briegel J, Manert W, Hummel T, et al. Health-related quality of life and posttraumatic stress disorder in survivors of the acute respiratory distress syndrome. Crit Care Med 1998;26(4):651–659.
63. Hopkins RO, Weaver LK, Pope D, Orme JF, Bigler ED, Larson-Lohr V. Neuropsychological sequelae and impaired health status in survivors of severe acute respiratory distress syndrome. Am J Respir Crit Care Med 1999;160(1):50–56.
64. Zapol WM, Snider MT, Hill JD, Fallat RJ, Bartlett RH, Edmunds LH, et al. Extracorporeal membrane oxygenation in severe acute respiratory failure. A randomized prospective study. JAMA 1979; 242(20):2193–2196.
65. Roberts TE. Economic evaluation and randomised controlled trial of extracorporeal membrane oxygenation: UK collaborative trial. The Extracorporeal Membrane Oxygenation Economics Working Group. BMJ 1998;317(7163):911–915; discussion 915–916.

Discussion

Hess: Let me share with you a problem that I encounter sometimes when I try to introduce evidence-based medicine into my practice. In the Gattinoni study they prone-positioned patients for up to 6 hours a day.[1] That's not what I would do in my practice. When we prone patients, we prone them all day long, and periodically, we turn them back into a supine position and see what happens. So it's difficult for me to say, based on the Gattinoni study, that I would not prone patients when how he conducted the study is quite different than my practice when I prone patients. Any comments about that?

REFERENCE

1. Gattioni L, Tognoni G, Pesenti A, Taccone P, Mascheroni D, Labarta V, et al. Effect of prone positioning on the survival of patients with acute respiratory failure. N Engl J Med. 2001;345(8)568–573.

Meade: Well, if you really believe in your strategy and you have good evidence to support it, then it might be worth conducting another trial. Proning is a difficult and controversial procedure, as you know, so if you're going to do it, it would be great to do it in the context of a research protocol, to evaluate your approach.

Rubenfeld: This is getting back to the issue about how we interpret evidence, and this is kind of the Bayesian point I was making earlier. Dean has a very different "prior" based on his clinical experience—his systematic observed experience of patients; none of it's published because we're not in that phase with proning. But he looks at the Gattinoni trial very differently than I do, because I come from a very different place. I'm not making a point about proning; I'm trying to make a point about thinking about evidence. From the same data and the same study, readers will come to very different conclusions—not about the validity of the study (though we may have different opinions about that too), but people come into the study with different priors, and I'm not sure that this is a bias. This is not one of those cognitive thinking things; it's just that they have different "priors" about the kind of treatment they use, and they come out with very different conclusions about the results.

MacIntyre: We're talking about proning as if it's an on-off situation, but, in fact, there's proning for 12 hours; there's proning for 18 hours; there's proning alternating with supine every few hours; there are all kinds of different ways. The problem we get into is that when a study comes out that does it one way, we tend to generalize the specific techniques as representing the overall concept—that proning either is or is not good.

Meade: Well, I can provide you with an approach. If there's a truly negative study that is statistically significant, or a truly positive study, and you simply do not agree with the results, then be careful about discarding the results altogether. Chances are that the "truth" is similar in direction but different in magnitude with modifications to a protocol. The story with proning is a little different—it's an underpowered study. So in this situation the investigators have probably neither ruled out the potential that proning offers a survival benefit nor ruled out the possibility that proning results in harm. So it's worth doing further studies, if there's good physiologic rationale.

Rubenfeld: It's a study with a likelihood ratio of about 1, so if I'm Dean Hess and I come to that study from whatever prior thinking that proning is a good thing and they just got it wrong, I'm probably going to keep doing it. I'm not saying that's bad or wrong, or that there's something bad about evidence-based medicine. It's just, for me, a different way of thinking about how we can look at the same evidence and disagree, not about the validity of the study or on our appraisal of it, but on what we do based on it.

Hess: I think the study was *very* well done, and I think the results are valid. I just don't think it's consistent with my practice.

Rubenfeld: Wrong dose.

Hess: Wrong dose.

MacIntyre: May I go back to your meta-analysis of the 4 lung protective strategies? Maureen, you're obviously well known as an evidence-based physician. A good evidence-based practice recommendation based on that meta-analysis would be that tidal volume doesn't make any difference. So are you saying that you believe there is no evidence to support a lung-protective strategy, based on your meta-analysis?

Meade: I conducted this pooled analysis a few days ago and was shocked to see that the random effect model of pooling the data showed no treatment effect. But I do believe that the ARDS Network trial differs from the other trials in some important ways. One is the management of acidosis. And, as you folks have pointed out, the difference between the control group's and experimental group's tidal volumes and airway pressures was much greater in the ARDS Network trial. That's why I don't think we should necessarily be pooling data.

MacIntyre: Let me push you harder then. Are you going to publish this meta-analysis?

Meade: This is not actually a meta-analysis. This was a spur-of-the-moment, thought-provoking pooling of results across 4 studies which, as I said, I'm not sure is valid. We may publish this sometime, but there is a lot of work to do first. We need to establish a priori hypotheses, consult with respiratory physiologists, and take a hard look at the data with an experienced meta-analyst such as Gordon [Guyatt].

MacIntyre: A fundamental principle behind meta-analysis is that the studies were similar, that the treatment strategies and control groups were similar. We talked earlier about how they are often different in the different trials. Specifically, the control group in all the trials in your meta-analysis, other than the ARDS Network trial, did not have as stiff a lung, in the sense that tidal volume strategy was not pushing them to an end-inspiratory "stretch" that, at least physiologically, would be dangerous.

Durbin: I'm glad we're into this discussion, because I'm still somewhat of a disbeliever in the methodologies.

Meade: Of meta-analysis?

Durbin: Of the whole process of using a meta-analysis approach to finding out answers to complex questions. How can I be sure the meta-analyzers were careful about how they choose the studies they included and how accurate and consistent is the methodology of each of the individual studies? Or, on a simpler level, how well are

they reported? Often studies are excluded because there isn't enough information published to allow analysis. Where is the bias correction for the person who's looking at studies? Inclusion isn't just based on how good the study is. There may be an author bias in choosing which studies to look at more carefully, and there may be an innate publication bias in publishing studies that are more likely to show effects than ones that don't. Therefore, there are not as many published studies to choose from to support one side of an issue.

Meade: Well, there are a ton of narrative reviews and systematic reviews (or what are called systematic reviews) out there that are not so great. And it's hard to know in those situations whether or not you can believe the result. Sometimes the results are correct, but their approach may not be great. But you can recognize really great meta-analysts by their methods. They are explicit about their methods, their questions, their search strategies, their inclusion and exclusion criteria, and about how they abstract the data. They demonstrate reproducibility in their assessment of eligibility in data abstraction. They explain the analysis, show you what the results are for all the studies, and they show you a critical appraisal of all the studies. So they do a really "fair" job. They apply the scientific method as best they can to the task at hand. And when folks do that, then you know they've done a good job and you can believe the results. And the results will only be as good as the studies that are going into the meta-analysis. If they don't do that, then it's hard to tell.

Durbin: We started out early this morning talking about studies that had 40,000 patients to answer simple questions such as whether to give aspirin or not following a myocardial infarction. And we said that now we've got to teach everybody to do what we know is true. Now we're talking about studies that have less than 1,000 patients, and maybe 4 or 5 studies that may meet criteria to be even analyzed in this way. Yet there's a move afoot by some people to have us all adopt a strategy of low-volume, low-pressure ventilation, based on what I think is insufficient evidence. I think it will be helpful to have your meta-analysis out there, because I think we need to continue to study these issues until we have more definitive answers.

Meade: I just don't know if that meta-analysis would be misleading, so I'd have to go back and do the work I mentioned earlier.

Flemons: When it comes to meta-analysis, it seems to me there's a bias that perhaps the most rigorous methodology doesn't address (though maybe it could) and that's the bias of deciding how much difference there is between the studies so you can decide whether to pool them. This strikes me as a good example; if you decide, physiologically, that the way the 2 studies treated the acidosis was different and therefore you can't pool them, then you get one answer. But if you decide the difference is not as important, you could then pool the results and get a different answer. So how do you take that into account? As far as I can see, you can't estimate that bias in terms of the people who are doing the analysis for the reader.

Meade: I don't want you to consider this pooling of results as a meta-analysis. It was a "back-of-the-envelope" analysis that I did a couple of days ago. A real meta-analysis—a good one—will include tests for heterogeneity between studies and will include collaboration with real experts in the field, which in this case would be an intensivist and a pulmonary physiologist, to decide if the differences between the studies are important with respect to treatment and management of acidosis. And in a good meta-analysis you'll see a discussion of why it was appropriate to pool, even if there were some differences among the studies. If a meta-analysis doesn't have that discussion, then it's a problem.

Ellrodt: One concern I'm hearing here is sort of evidence-paralysis, where you keep thinking you need a perfect study or you need this or that, and I think you have to be careful that you don't get into this paralytic state where you don't make a decision one way or another about whether you're going to proceed or not. Let me give you the down side of that. For example, going back to one of Gordon's [Guyatt] first slides, which was the thrombolytic slide, where people just weren't acting on the thrombolytic information. You could go through every year how many thousands of lives were lost because people were not acting. So I just want people to be careful not to be sitting there saying "I don't know this, I don't know this." At some point you're going to have to make a decision, and I'm just going to give you mine on ARDS: I'm going to take the best trial. I'm going to be controversial here. I'm going to jump on the ARDS Network trial and say, "That makes sense to me." I think, until you prove me wrong, that low-volume, low-pressure ventilation makes sense. And I think I'm going to be saving a lot of lives if I do that right, and I could figure out how many there are that I could be saving, and I'm going to do it that way until you prove to me that it's harmful. I think you need to not be paralyzed by this stuff and say, "We need another trial." Every study that's ever done ends with a call for more research.

Meade: The important thing is that we're aware of this evidence. The intensivists here are aware of the 4 studies, and have evaluated them. We know the point estimates from each one. We know what happens if you pool; we know about the potential problems with pooling; and as Gordon was say-

ing this morning: it all comes down to judgment, especially when the waters are more murky. We all make our own value judgments about whether we should be using pressure- and volume-limited ventilation.

Ellrodt: What do you do?

Meade: I use pressure- and volume-limited ventilation, but I use a more "open lung" approach than the ARDS Network protocol included.

Ellrodt: What does everybody around this room do? How many people follow the ARDS Network protocol?

Rubenfeld: What do we *do* or what do we *say* we do?

Ellrodt: What do you *try* to do?

Meade: I have traveled across Canada to present a large ongoing ventilation study. Everyone says they follow the ARDS Network protocol, but when it comes to *implementing* it in the control group of our current study, I can tell you there are a lot of surprises in these centers; they haven't been doing it.

Guyatt: I'd like to clarify this point about when do you pool and when do you not pool results and Ward's [Flemons] point about the bias that could be introduced. In terms of Maureen's excellent list of what makes a good meta-analysis, one additional point is the development of a priori hypotheses about why results might differ from trial to trial. One strategy—and personally I think the best solution to the problem that Ward laid out—is to pool widely, but start with some a priori hypotheses as to what may explain differences across study results, and then to test them. In this instance I would say go ahead and meta-analyze. You folks have given us an a priori hypothesis: the differences in study results may be due to the controlled ventilation strategy and the high pressures that result. That would be an *apparent* explanation. That, perhaps, has some implications, one being, as Maureen was saying, that people have *great* difficulty implementing the ARDS Network protocol. If the problem really is the very high control pressures, then maybe you don't need to go quite so low and run into all those problems. The bottom line of this is that the additional meta-analytic tool is a priori hypotheses about what might explain differences in studies, and exploration of those in the analysis phase of the meta-analysis.

Ellrodt: If you talk about "voltage drops" from the evidence to practice (and a number of you were getting at this), it's amazing how it happens. Let me give you an example, from the Canadian Consensus Statement about indications for cesarean section, done back in the 1980s.[1] It was amazing the way this worked: 90% of Canadian obstetricians studied were aware of the consensus statement, which is a pretty high awareness, and 90% *agreed* with the recommendations, which was pretty amazing too. Probably only about 3% were familiar enough with the recommendations that they could answer specific questions about them. Now there's a real problem, right there. But when they asked, "How many of you actually practice this way?" (as opposed to merely agreeing with it) the number dropped to 33%. And when they looked at the charts to see what was actually happening, almost no one was practicing according to the recommendations. So there are multiple voltage drops along the way, and I sometimes have a greater concern about that than how good the meta-analysis is. It's important to get it right, of course, but, boy, even starting there, things fall apart. This is what you're finding, for example, in your study across Canada, I think. It's certainly been seen in supine versus semi-recumbent ventilation, where everybody says, "Yeah, I believe that's true, and yeah, I'm ventilating at 45°," but you look at the patient and it's 2° or something like that.

So I think there's a lot more to it, and I think you have to think of those voltage drops all the way along the line. The final voltage drop, which we don't talk about, is patient compliance with EBM recommendations. For many situations in the ICU, you have the patients "hostage" so to speak, and they don't have a lot of say over whether they have an intervention done or not. But when you start talking about long-term therapies for conditions such as asthma, medication adherence, adherence to exercise, and things like that, there's a *huge* drop-off at that point. And we wonder why things don't work as they do in the literature. I think the last thing we really need to talk about is patient compliance and how we can modify or improve patient adherence to evidence-based recommendations.

REFERENCE

1. Indications for cesarean section: final statement of the panel of the National Consensus Conference on Aspects of Cesarean Birth. CMAJ 1986;134(12):1348–1352.

Evidence-Based Treatments for Acute Asthma

Brian H Rowe MD MSc, Marcia L Edmonds MD MSc, Carol H Spooner BScN MSc, and Carlos A Camargo MD DrPH

Introduction
In-Emergency Department Care
- **β Agonists**
- **Anticholinergics**
- **Systemic Corticosteroids**
- **Magnesium Sulphate**
- **Inhaled Corticosteroids**
- **Other Therapies**

Post-Emergency Care
- **Oral Corticosteroids**
- **Inhaled Corticosteroids**
- **Other Therapies**

Non-Pharmacologic Approaches
- **Asthma Education**
- **Other Issues**

Summary

Asthma is an important health care problem; over 12 million people in the United States suffer from asthma, the majority of whom are young patients. Presentations of acute asthma to emergency departments are common. In the United States, acute asthma presentations account for close to 2 million emergency department visits annually, and these patients often exhibit acute and chronic markers of severe asthma; so controlling asthma is important from many perspectives. We review the evidence for various acute asthma therapies, using the highest levels of evidence, employing systematic reviews (especially those from the Cochrane Collaboration) and evidence from randomized controlled trials to guide therapy decisions. β agonists and systemic corticosteroids are the cornerstones of initial treatment. Delivery of β agonists via nebulizer or metered-dose inhaler with spacer device appear to be similarly efficacious. However, recent evidence from studies involving children and adults indicate that addition of ipratropium bromide to early β agonist treatments may reduce airway obstruction and reduce hospital admissions, especially for more severe asthma. Evidence from systematic reviews indicates that intravenous magnesium sulfate may provide similar benefits in severe asthma. Antibiotics, intravenous β agonists, and intravenous aminophylline have been shown to add little and may increase adverse effects. Treatment for discharged patients should include systemic corticosteroids for 5–7 days, for all but the mildest asthma. Addition of inhaled corticosteroids should be considered for most patients, since evidence suggests that inhaled corticosteroids may reduce relapses and improve quality of life. Alternative treatments such as long-acting β agonists and leukotriene antagonists remain unproven in this setting. Linking a discharge plan to close follow-up and asthma education (especially an action plan) needs to be encouraged. Acute asthma is a common problem and treatment has improved dramatically over the past 10 years. Employing the evidence-based practice outlined above should reduce the burden of acute asthma on patients and the health care system. *Key words: evidence-based medicine, asthma, emergency medicine, corticosteroids, relapse, admission.* [Respir Care 2001;46(12):1380–1390]

Introduction

Asthma is a particularly important health care problem in both Canada and the United States. Over 12 million people in the United States suffer from asthma, and the majority of those are young patients, most under the age of 18.[1] In fact, asthma affects nearly 7% of children and 5% of adults in North America.[1] The costs associated with asthma are staggering: in 1990 the indirect and direct expenditures for asthma exceeded $6 billion in the United States[2] and nearly $600 million in Canada.[3] In Canada, acute asthma (emergency department [ED] visits and hospitalization) accounts for approximately 25% of the total costs associated with asthma care.

Presentations of acute asthma to EDs and other settings are common. In the United States, acute asthma presentations account for close to 2 million ED visits annually,[4] which are precipitated by many factors, the most common being superimposed upper respiratory tract infection, environmental allergies, and poor control of chronic asthma. ED visits are important events for asthmatics and their families, as they represent a vulnerable point in the illness and are associated with substantial morbidity and occasional mortality. Moreover, in spite of adequate care, a patient who suffers an exacerbation may feel its consequences and suffer relapses for weeks after the initial ED visit. For those reasons, the assessment and treatment of acute asthma has been the focus of considerable research and clinical practice guideline development efforts.[5,6] However, despite those national attempts to standardize and improve asthma care, there remain wide gaps between what is known and what is practiced,[7] most of which are related to physician variability in diagnosis and treatment.

Brian H Rowe MD MSc, Marcia L Edmonds MD MSc, and Carol H Spooner BScN MSc are affiliated with the Division of Emergency Medicine, University of Alberta, Edmonton, Alberta, Canada. Brian H Rowe MD MSc and Marcia L Edmonds MD MSc are also affiliated with the Capital Health Authority, Edmonton, Alberta, Canada. Carlos A Camargo MD DrPH is affiliated with the Department of Emergency Medicine, Massachusetts General Hospital and Channing Laboratory, Department of Medicine, Brigham and Women's Hospital, Harvard Medical School, Boston, Massachusetts.

Brian H Rowe MD MSc is supported by a salary award from the Government of Canada as the Canada Research Chair of Emergency Airway Diseases. Carlos A Camargo MD is supported by grant HL-03533 from the National Institutes of Health.

A version of this report was presented by Brian H Rowe MD MSc at the Respiratory Care Journal Conference, Evidence-Based Medicine in Respiratory Care, April 20–22, 2001, Banff, Alberta, Canada.

Correspondence: Brian H Rowe MD MSc, University of Alberta, Division of Emergency Medicine, 1G1.63 Walter C Mackenzie Centre, 8440 112 Street, Edmonton, Alberta T6G 2B7, Canada. E-mail: brian.rowe@ualberta.ca.

Treatment of acute asthma includes severity assessment, in-ED treatment, post-ED treatment, and follow-up. To begin with, treating acute asthma requires a comprehensive history and physical examination on the part of the provider. To accurately assess the severity of an asthma attack, the physician should know the patient's asthma history (including intubation, hospitalizations, and recent exacerbations), medication use (eg, "relievers" and "controllers"), current pulmonary function test results (peak expiratory flow [PEF], forced expiratory volumes, or both), vital signs (including blood oxygen saturation measured by pulse oximetry), and chest examination findings.

Selecting the most effective medication protocol for treating acute asthma has been the subject of considerable study. Herein we summarize research results on the main pharmacologic and nonpharmacologic approaches to the treatment of asthma exacerbations. In doing so we rely heavily on systematic review evidence from the Cochrane Collaboration. These systematic reviews use standardized and rigorous methods to summarize and combine the best evidence from individual randomized controlled trials pertaining to specific topics. The results represent Level I evidence for treatment decisions.[8] In particular, the reviews from the Airway Review Group have been extensively quoted and routinely regarded as high quality.[9]

In-Emergency Department Care

The goal of in-ED care is to safely and effectively treat the acute bronchospasm associated with the presentation and to initiate anti-inflammatory therapy. The approaches described should reduce the need for hospitalization and ensure that patients receive the appropriate therapy to prevent relapse and reduce the potential for a serious negative outcome (eg, intubation or death).

β Agonists

Early treatment of acute asthma has generally focused on the use of inhaled (usually via nebulizer) short-acting β_2 agonists because of their undisputed, generally rapid effect of relieving bronchospasm and associated breathing dysfunction. Whether the drug is most effective when delivered via nebulizer or via metered dose inhaler with holding chamber/spacer (MDI/HC) has been an area of intense research. A systematic review in the Cochrane Library suggests that those delivery methods yield similar outcomes.[10] For example, pooled results (Fig. 1) indicate that MDI and nebulizer produce similar admission rate (odds ratio [OR] 1.0, 95% confidence interval [CI] 0.54–1.85) and show no important differences in PEF (mean difference in percent of predicted PEF 1.3%, 95% CI -2–5%). Economic evaluations of nebulizer versus MDI/HC favor MDI/HC.[11] Finally, the use of MDI/HC was associated

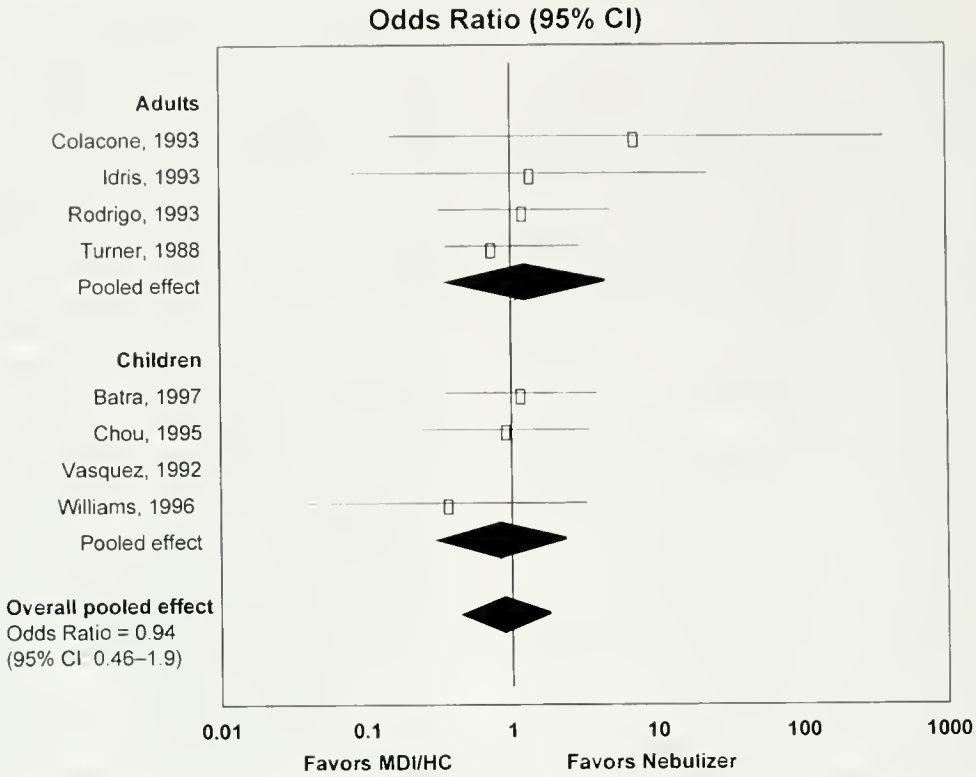


Fig. 1. Effect of β agonists on hospital admissions for acute asthma, based on delivery via nebulizer or metered-dose inhaler with holding chamber (MDI/HC) and stratified by age (adults vs children). CI = confidence interval. (Adapted from Reference 10, in which individual citations in the figure are identified.)

with fewer adverse effects (eg, tachycardia), especially in children. However, those data do not include patients with life-threatening severe asthma. From a clinical perspective, these results suggest using MDI/HC in asthma patients who present with mild to moderate symptoms. For patients with severe asthma, the benefits and ease of continuous nebulization and the need to focus on other issues may make nebulization an attractive alternative.[12] Finally, employing MDI/HC delivery in the acute setting affords an opportunity to assess the patient's inhaler technique and to educate the patient with regard to appropriate care.

Attempts to identify optimal doses or treatment intervals to achieve maximum bronchodilation or symptom relief have not been successful. However, continuous treatment may have an advantage over intermittent treatment in severe asthma.[13] In addition, lower doses appear to be equivalent to higher doses with regard to maximizing bronchodilation or clinical outcome.[14] A substantial number of patients achieve a bronchodilation "plateau" and in those people additional β_2 agonist therapy only seems to cause more adverse effects. Some guidelines now recommend that β agonists be titrated to plateau using objective assessment of airway obstruction with pulmonary function measures.[5]

Anticholinergics

There is increasing support, particularly for children, for adding anticholinergic agents (ipratropium bromide) to β_2 agonist therapy in moderate to severe acute asthma.[15,16] A systematic review involving children compared ipratropium bromide plus β_2 agonists to β_2 agonists alone.[15] Summary statistics indicate that multiple doses of ipratropium bromide effect a clinically important improvement in forced expiratory volume in the first second (FEV_1): 16.1% at 60 minutes (95% CI 6–27%) and 17.5% (95% CI 4–31%) at 120 minutes. The combined therapy reduced the risk of hospital admission by 25% (relative risk [RR] 0.75, 95% CI 0.62–0.89) in moderate and severe exacerbations. The number needed to treat to prevent 1 admission was 12 (95% CI 8–32), and the number needed to treat decreased to 7 in severe cases. Those results were confirmed by the largest individual trial involved in an updated Cochrane review.[17] There was no conclusive evidence for single or multiple doses of ipratropium bromide in children with mild exacerbations. Neither therapy group was associated with substantial adverse effects.

A similar meta-analysis in adults also indicated a modest beneficial effect from adding ipratropium bromide to

inhaled β_2 agonists.[16] The absolute increase in FEV_1 was 7.3% (95% CI 4–11%) over 45–90 minutes. The absolute increase in PEF was 22.1% (95% CI 11–33%) over 45–90 minutes. The risk of admission was 27% lower (RR 0.73, 95% CI 0.53–0.99). A large randomized controlled trial has since been completed that confirms the systematic review evidence.[18] The study observed a 21% (95% CI 3–38%) improvement in PEF and a 48.1% (95% CI 20–76%) improvement in FEV_1 over the control group. High doses of ipratropium bromide reduced the risk of hospital admission by 49% (RR 0.51, 95% CI 0.31–0.83). The number needed to treat to prevent 1 admission was 5 (95% CI 3–17). Although questions such as the dose-response relationship still need to be resolved regarding ipratropium bromide therapy in the ED setting, it seems prudent to use this agent with β_2 agonists for patients with moderate to severe acute asthma.

Systemic Corticosteroids

The airway edema and secretions associated with acute asthma are most effectively treated with anti-inflammatory agents such as corticosteroids. The early use of systemic corticosteroids (ie, within 1 h of ED presentation) delivered orally or intravenously continues to be a principal treatment choice in published evidence-based asthma guidelines.[5,6] A meta-analysis investigating this issue determined that the early use of corticosteroids for acute asthma in the ED significantly reduced admission rates (OR 0.40, 95% CI 0.21–0.78). The number needed to treat was 8 (95% CI 5–21).[19] This benefit was more pronounced for those not already receiving systemic corticosteroids (OR 0.37, 95% CI 0.19–0.70) and those experiencing a severe exacerbation (OR 0.35, 95% CI 0.21–0.59). Adverse effect profiles were similar among all systemic corticosteroids treatment routes and placebo.

The debate regarding the use of intravenous versus oral corticosteroids in the ED persists but now seems to be focused on identifying which patients require the intravenous route, as opposed to the oral route. None of the evidence from controlled trials or meta-analyses suggests that the advantage offered by steroids in moderate to severe asthma is related to the route of administration. Further systematic review evidence on dosing suggests that high-dose corticosteroids, at least in hospitalized patients, are no more effective than moderate doses.[20]

Applying this information to practice requires a clear understanding that not all levels of severity have been assessed with sufficient rigor to confirm equivalency of systemic routes in all situations. Until further evidence is available, it seems reasonable to select oral agents as the first-line choice, while reserving intravenous corticosteroids for patients who are too dyspneic to swallow, are obtunded or intubated, or are unable to tolerate oral medications (eg, vomiting).

Magnesium Sulphate

The use of magnesium sulfate in unresponsive acute asthma has gained support recently. There have been a number of systematic reviews, which concluded that intravenous magnesium is not only safe but also effective in patients with severe asthma.[21,22] The Cochrane review on this subject[21] found that the addition of intravenous magnesium sulfate reduced hospitalization (Fig. 2) (OR 0.1, 95% CI 0.04–0.27) and improved pulmonary function (mean increase in PEF 52 L/min, 95% CI 27–77) in severe asthma more than did β agonist and intravenous systemic corticosteroids only. Overall, there were no changes in systolic blood pressure with the addition of magnesium sulfate, and adverse effects were rare or minor. It is important to note that the *routine* use of magnesium sulfate in all asthma patients did not produce clear beneficial effects (OR for admission 0.31, 95% CI 0.09–1.04). Patients with clinically severe asthma and/or pulmonary function test results $< 30\%$ of predicted in adults and $< 50\%$ in children, and who exhibit a poor response to initial bronchodilator therapy, may benefit most from intravenous magnesium sulfate treatment. Since this agent has been shown to be easy to use, extremely safe, and inexpensive, its early use in severe acute asthma should be considered. Currently the recommended dose is 2 g intravenous over 20 minutes in adults and 25–100 mg/kg in children (total maximum dose of 2 g).[21]

Inhaled Corticosteroids

Though inhaled corticosteroids are usually considered a therapy for chronic asthma, in which beneficial effects are seen over a prolonged period, there is emerging evidence supporting their use in the ED setting for acute asthma. A Cochrane systematic review suggests that inhaled corticosteroids may reduce admissions to hospital and improve pulmonary function when administered early in the ED protocol.[23] Employing inhaled corticosteroids in acute asthma was associated with fewer admissions (Fig. 3) (OR 0.33, 95% CI 0.17, 0.64) and more improvement in pulmonary function (mean difference PEF 8.0%, 95% CI 3–13) than placebo. However, several of the studies included in that review did not administer systemic corticosteroids to either the treatment or control group, thus limiting the power of the review to determine the additive benefit of inhaled corticosteroids when systemic corticosteroids are being used.

A recent study[24] indicates that there may be drawbacks to replacing oral corticosteroids with inhaled corticosteroids in the treatment of acute asthma. In that randomized

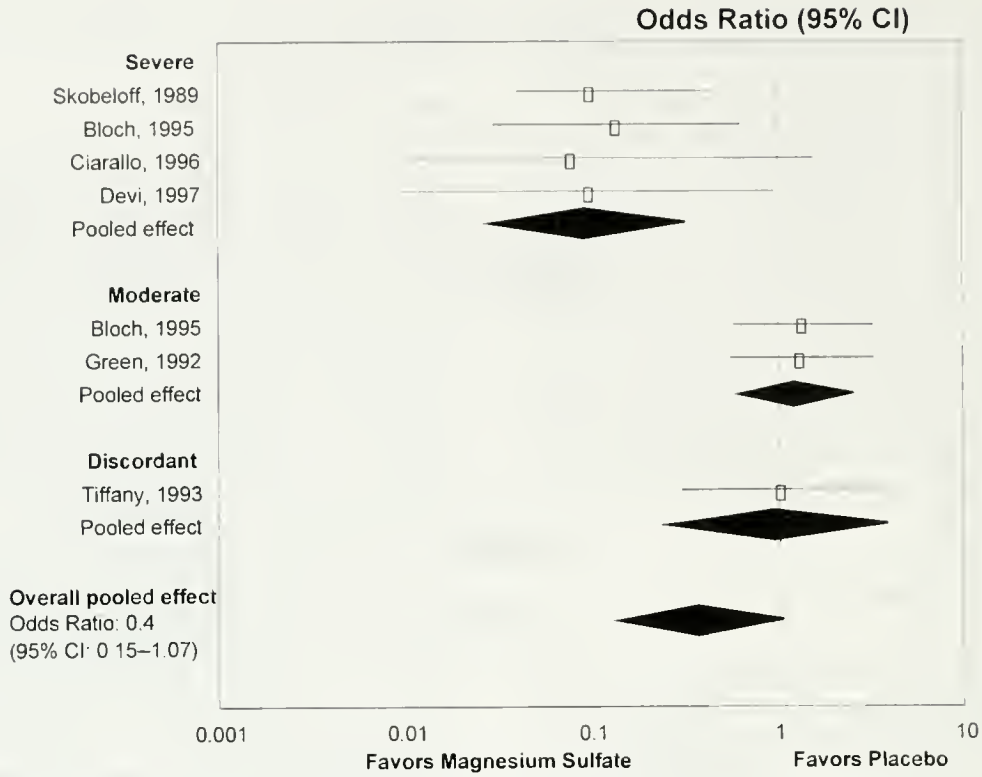


Fig. 2. Effect of intravenous magnesium sulfate versus placebo on hospital admissions for acute asthma, stratified by level of severity. CI confidence interval. (Adapted from Reference 21, in which individual citations in the figure are identified.)

double-blind study, patients received either inhaled corticosteroids or oral corticosteroids in addition to standard β_2 agonist therapy. Those treated with oral corticosteroids performed better and were admitted less frequently than those treated with inhaled corticosteroids. Combined with the previous meta-analysis data, those results suggest that inhaled corticosteroids may be useful as an adjunct to systemic corticosteroids, but not as a replacement choice.[23,25] Additional research is needed to determine the optimal dose, frequency, and drug to be used, and to clarify the magnitude of the additional benefit when oral corticosteroids are being administered concurrent with inhaled corticosteroids.

Other Therapies

The benefit of other agents, such as aminophylline,[26] intravenous β agonists,[27] and heliox[28] remains limited. None of the Cochrane systematic reviews found beneficial effects associated with those agents. Moreover, for β agonists[27] and aminophylline[26] the adverse effects clearly outweigh the benefits. Antibiotics should not be used unless community-acquired pneumonia is complicating the asthma.[29,30] Evidence for or against the use of newer agents such as leukotriene modifiers and levalbuterol remains unclear at this point, but current research should help to clarify the place of those agents.

Post-Emergency Care

The goal of post-ED care is to safely return each patient to a level of functioning commensurate with the current definition of asthma "control." According to the Canadian guidelines, control means the patient is using rescue β agonists fewer than 4 times per week, is sleeping through the night, and is performing his or her regular daily activities (eg, work, exercise) without limitations due to asthma.[5] This would also entail patients receiving the appropriate therapy (eg, medications, education compliance) required to prevent or attenuate the next asthma exacerbation.

Oral Corticosteroids

Approximately 12–16% of patients treated for acute asthma will relapse within 2 weeks of ED discharge, many because of unresolved inflammation that leaves the airways sensitive to inhaled irritants.[31] Guidelines strongly encourage treatment with systemic corticosteroids following ED discharge for an acute exacerbation, to reduce the

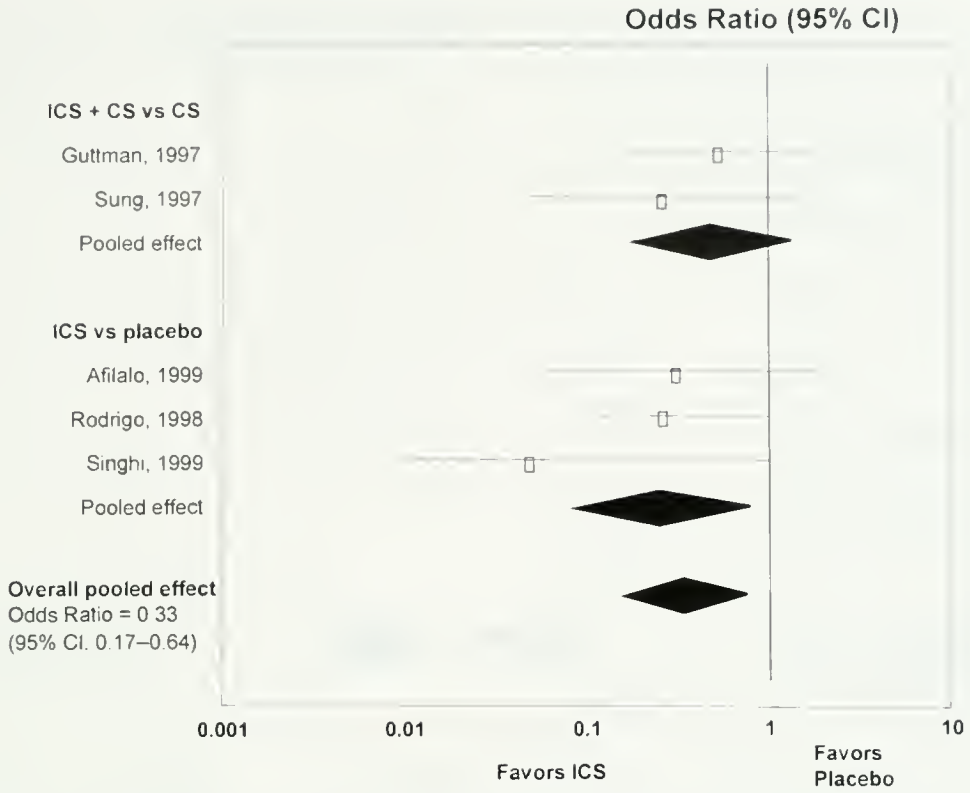


Fig. 3. Effect of inhaled corticosteroids (ICS) on hospital admissions for acute asthma, based on comparisons of ICS plus systemic corticosteroids versus systemic corticosteroids alone (ICS + CS vs CS) and inhaled corticosteroids versus placebo (ICS vs placebo). CI = confidence interval. (Adapted from Reference 23, in which individual citations in the figure are identified.)

risk of relapse.[5,6] Compelling evidence for that approach is found in a Cochrane systematic review comparing post-ED corticosteroids therapy to placebo.[31] Significantly fewer patients in the corticosteroids group relapsed in the first week (Fig. 4) (OR 0.35, 95% CI 0.17–0.73). That reduced risk continued over the first 21 days (OR 0.33, 95% CI 0.13, 0.82). The corticosteroid group also had less need for β_2 agonists (mean difference 3 activations/d, 95% CI -5.5 to -1.0). Pulmonary function test results and adverse effects, though rarely reported, were not different between the treatment groups. Quality of life was not reported frequently enough to comment on this outcome. A subgroup analysis indicated that intramuscular corticosteroids and a 7–10 day tapering course of corticosteroids were similarly efficacious. Intramuscular therapy may be best reserved for patients with questionable compliance, inability to afford the price of an oral prescription, or those who are otherwise unreliable (eg, cognitive impairment, intoxication). The review determined that the associated number needed to treat was 10 (95% CI 7–22) treated patients to prevent 1 relapse after an asthma exacerbation.[31]

The small sample sizes of the randomized controlled trials performed to date did not permit an examination of the relative effectiveness of various regimens, and a definitive recommendation cannot be provided concerning dose or dosing protocol(s). However, given the better compliance associated with the once-daily dose and the availability of 40 or 50 mg tablets in North America, the use of oral corticosteroids for a short period (5–10 d) seems appropriate for most patients discharged after an acute asthma episode. Tapering oral corticosteroids over the first 7–14 day period appears unwarranted,[32,33] especially when inhaled steroids and other anti-inflammatory agents are administered concurrently.[34]

Inhaled Corticosteroids

In North America, the majority of patients with acute asthma treated in an emergency setting are discharged and prescribed a short course (5–7 d) of oral corticosteroids. Less information exists regarding the use of inhaled corticosteroids; however, the data that exist indicate impressive practice differences with respect to that treatment. For example, in United States sites associated with a large North American ED airway research network, only 10% of discharged patients were prescribed an inhaled corticosteroid if they were not regularly taking one, whereas in Canadian sites more than 50% of similar patients were treated with an inhaled corticosteroid at discharge.[35]

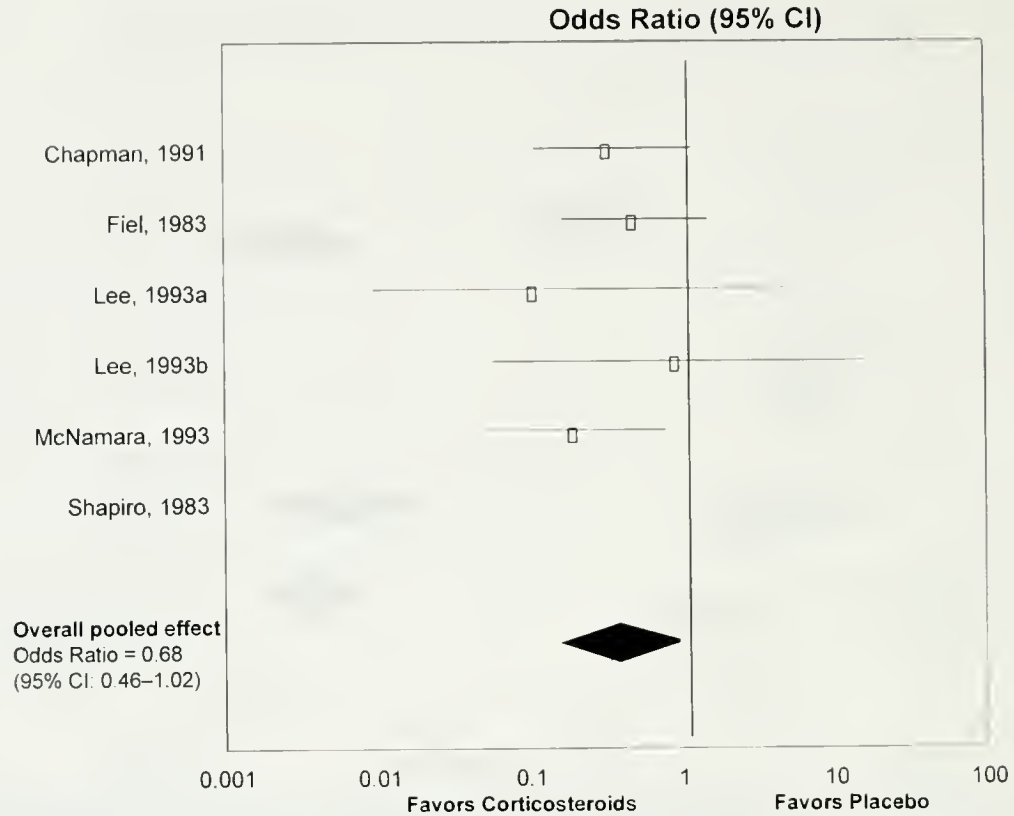


Fig. 4. Effect of corticosteroids (versus placebo) on subsequent relapse in acute asthma. CI = confidence interval. (Adapted from Reference 31, in which individual citations in the figure are identified.)

There is evidence to support using a combination of inhaled and oral corticosteroids after discharge from the ED.[34] There are 2 published randomized controlled trials[34,36] and one in press[37] that individually provide somewhat conflicting evidence on the addition of inhaled corticosteroids, but when combined in a systematic review favor the combination.[38] The pooled effect indicates a trend of fewer post-discharge relapses among the group that used inhaled corticosteroids plus oral corticosteroid than among those who used only oral corticosteroids (Fig. 5) (OR 0.68, 95% CI 0.46–1.02).[38]

Clinically, the results of that review indicate that patients who are already taking inhaled corticosteroid agents should be counseled by the ED staff regarding compliance-enhancing interventions.[39–41] Keep in mind that many of the acute asthma patients who present to the ED exhibit features associated with poorly controlled chronic asthma.[41] They represent vulnerable patients who are ideal candidates for inhaled corticosteroids. Consequently, we would recommend those patients not already on inhaled corticosteroids agents be considered for short or long-term inhaled corticosteroid therapy in conjunction with oral prednisone after discharge. The dose and duration of inhaled and oral corticosteroids should be based on recent history of symptom control, health care utilization, and quality of life indicators. For those patients with more severe illness, this clearly would be the optimal treatment strategy.

There are several recent publications examining the effect of replacing oral corticosteroids with high-dose inhaled corticosteroids. These generally compare oral prednisone to very high doses of inhaled corticosteroids in acute mild asthma after discharge. Though the systematic review found no significant difference in asthma relapse between the two treatments (OR 1.0, 95% CI 0.48–1.42), those results need to be interpreted cautiously.[38] Although the evidence implies equivalence, the results are not conclusive, because of the width of the CIs and the inclusion of only patients with mild asthma exacerbations. Given the limited data on this issue to date, use of inhaled corticosteroids alone should be reserved for those patients with very mild asthma and those who refuse to or cannot take oral corticosteroids. Compared to the traditional short course of prednisone, inhaled corticosteroids are expensive and more difficult for patients and families to use. Given the potential for added benefit with combined therapy, future research should focus on that important comparison.

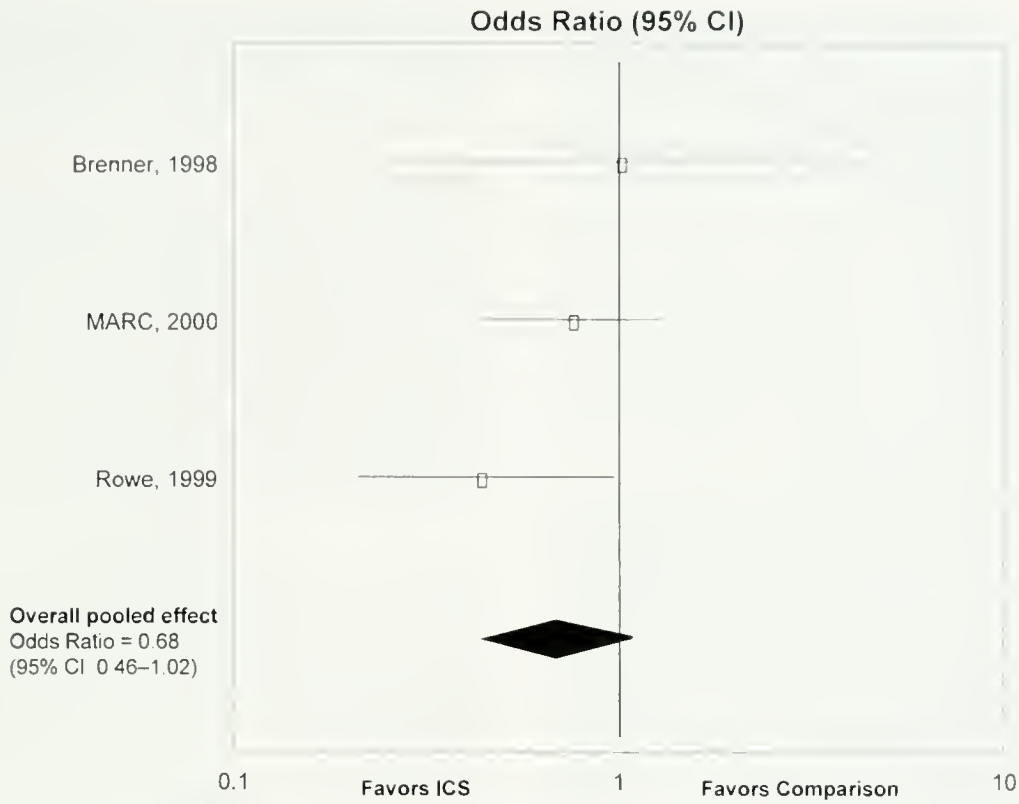


Fig. 5. Effect of adding inhaled corticosteroids (ICS) (versus corticosteroids alone) on subsequent relapse in acute asthma. CI = confidence interval. (Adapted from Reference 38, in which individual citations in the figure are identified.)

Other Therapies

Exciting advances are being made in chronic asthma care with the introduction of long-acting β agonists[42] and leukotriene modifiers.[43] Though preliminary evidence suggests those agents may be effective in the acute setting, further evidence of both efficacy and effectiveness are required prior to recommending implementation.

Non-Pharmacologic Approaches

Asthma Education

Education is one of the key recommendations in the North American asthma guidelines.[5,6] In addition, surveyed emergency physicians felt that education was an important component of asthma care and rated many education items as necessary.[40] In a narrative review of asthma education, authors have emphasized the need to educate asthma patients.[44] However, overall, the results of individual trials and systematic reviews regarding general asthma education have been disappointing; this is especially true for the acute setting.

A systematic review of randomized controlled trials with children who attended the ED was conducted to identify whether asthma education leads to improved health outcomes.[45] The analyses found that structured education, as compared to usual care or lower intensity education, did not reduce subsequent ED visits (RR 0.87, 95% CI 0.37–2.08), hospital admissions (RR 0.74, 95% CI 0.38–1.46), or unscheduled doctor visits (RR 0.74, 95% CI 0.49–1.12). However, there was substantial heterogeneity in the pooled results ($p < 0.01$), with potential for uncontrolled influence from several confounding factors. The authors concluded that there was no firm evidence to support asthma education for children to improve asthma control and that more rigorous research was necessary.

Another Cochrane review examined the impact of limited asthma education programs (information only) for asthmatic adults.[46] There was no effect on hospital admissions, doctor visits, lung function, medication use, or normal activity days lost. Perceived asthma symptoms did improve in the education group (OR 0.40, 95% CI 0.18–0.86). One included study found that education was associated with fewer ED visits (mean decrease in visits/person/y 2.8, 95% CI -4.3–1.2). The reviewers concluded that use of limited asthma education as it has been practiced does not appear to improve health outcomes in adults. The usefulness of education in the ED was encouraging, but further research is required to confirm those findings.

A second review by the same group assessed the effects of adult asthma self-management programs coupled with regular medical review.[47] Self-management education reduced hospitalizations (OR 0.57, 95% CI 0.38–0.88), emergency room visits (OR 0.71, 95% CI 0.57–0.90), unscheduled doctor visits (OR 0.57, 95% CI 0.40–0.82), missed work/school days (OR 0.55, 95% CI 0.38–0.79), and nocturnal asthma (OR 0.53, 95% CI 0.39–0.72). Pulmonary function measures, however, changed very little with the combined interventions. If a written action plan was added to the program, there were even fewer hospitalizations (OR 0.35, 95% CI 0.18–0.68). Patients who could self-adjust their medications using an individualized written plan had better lung function than those whose medications were adjusted by a doctor.

The clinical implications of these reviews seem to be that isolated general asthma education alone provides limited benefit. However, management plans that involve regular review by health care professionals plus teaching patients to self-monitor and adjust their medications using a written action plan appear to be effective in reducing asthma symptoms, health care use, and improving asthma quality of life, and should be encouraged. Clinicians might be well advised to educate staff, patients, and families in asthma self-management that involves monitoring of asthma (by either PEF or symptoms), regular medical review, and provision of a written action plan.

Other Issues

Studies have documented that a large percentage of patients are repeatedly exposed to environmental irritants. A substantial number of asthma patients are either exposed to cigarette smoke or persist in smoking despite the presence of asthma. Smoking cessation counseling and avoidance strategies should be provided to those patients and their families, during every exacerbation, in an attempt to motivate smokers to overcome the addiction.

Acute exacerbations represent an opportunity for ED physicians and staff to review pharmacologic and nonpharmacologic asthma management. Adhering to a long-term plan to keep asthma under control is often problematic, especially in the areas of regular medication use and avoiding environmental triggers. The opportunity to introduce or reinforce helpful behaviors should not be lost. Whenever practical, physicians should encourage patients to seek continuing primary-care physician follow-up.

Other considerations, such as immunizations against influenza,[48] use of acupuncture,[49] homeopathy,[50] and dietary changes (such as fatty acid intake[51]) have been promoted in the past, but in the literature there is no evidence of benefit from those interventions and one should be cautious about recommending them. However, evidence linking obesity and asthma[52] suggests that it may be prudent to encourage a regular exercise program and weight reduction as part of any long-term asthma management plan.

Summary

Asthma is a common, chronic, and often debilitating disease. The new treatment approaches to control bronchial inflammation summarized herein provide hope for an early return to activities, reduced symptoms, and improved quality of life in the subacute period following an asthma exacerbation. Combining self-management skills and educational interventions with appropriate preventive medication provides patients with the best opportunity to maintain health status and prevent exacerbations or relapse.

ACKNOWLEDGEMENTS

The authors would like to thank Diane Milette for her secretarial support and to acknowledge the work of the staff (Stephen Milan, Toby Lasserson, and Karen Blackhall) and the editor (Paul Jones) of the Airway Review Group at St George's Hospital Medical School for permitting the publication of the figures and support with the development of reviews.

REFERENCES

1. Camargo CA Jr, Richardson LD. Epidemiology of asthma. In: Brenner BE, editor. Emergency asthma. New York: Marcel Dekker, 1998.
2. Weiss KB, Gergen PJ, Hodgson TA. An economic evaluation of asthma in the United States. N Engl J Med 1992;326(13):862–866.
3. Krahn MD, Berka C, Langlois P, Detsky AS. Direct and indirect costs of asthma in Canada. CMAJ 1996;154(6):821–831.
4. Mannino DM, Homa DM, Pertowski CA, Ashizawa A, Nixon LL, Johnson CA, et al. Surveillance for asthma–United States, 1960–1995. Mor Mortal Wkly Rep CDC Surveill Summ 1998;47(1):1–27.
5. Boulet L-P, Becker A, Berube D, Beveridge RC, Ernst P. Canadian asthma consensus report, 1999. Canadian Asthma Consensus Group. CMAJ 1999;161(11 Suppl):S1–S61.
6. National Asthma Education Program. Expert Panel Report II: Guidelines for the diagnosis & management of asthma. National Heart, Lung, and Blood Institute. 1997. Available at http://www.nhlbi.nih.gov/guidelines/asthma/asthgdln.htm. Accessed Oct 4, 2001.
7. Cabana MD, Rand CS, Powe NR, Wu AW, Wilson MH, Abboud PC, Rubin HR. Why don't physicians follow clinical practice guidelines? A framework for improvement. JAMA 1999;282(15):1458–1465.
8. Guyatt GH, Sackett DL, Sinclair JC, Hayward R, Cook DJ, Cook RJ. User's guide to the medical literature IX: A method of grading health care recommendations. Evidence-Based Medicine Working Group. JAMA 1995;274(22):1800–1804.
9. Jadad AR, Moher M, Browman GP, Booker L, Sigouin C, Fuentes M, Stevens R. Systematic reviews and meta-analyses on treatment of asthma: critical evaluation. BMJ 2000;320(7234):537–540.
10. Cates CJ, Rowe BH. Holding chambers versus nebulisers for beta-agonist treatment of acute asthma (Cochrane Review). In: The Cochrane Library, 3, 2001. Oxford: Update Software.
11. Turner MO, Gafni A, Swan D, Fitzgerald JM. A review and economic evaluation of bronchodilator delivery methods in hospitalized patients. Arch Intern Med 1996;156(18):2113–2118.

12. Gibbs MA, Camargo CA Jr, Rowe BH, Silverman RA. State of the art: therapeutic controversies in severe acute asthma. Acad Emerg Med 2000;7(7):800–816.
13. Shrestha M, Bidadi K, Gourlay S, Hayes J. Continuous vs intermittent albuterol, at high and low doses, in the treatment of severe acute asthma in adults. Chest 1996;110(1):42–47.
14. Stauss L, Hejal R, Galan G, Dixon L, McFadden ER Jr. Observations on the effects of aerosolized albuterol in acute asthma. Am J Respir Crit Care Med 1997;155(2):454–458.
15. Plotnick LH, Ducharme FM. Should inhaled anticholinergics be added to beta$_2$ agonists for treating acute childhood and adolescent asthma? A systematic review. BMJ 1998;317(7164):971–977.
16. Stoodley RG, Aaron SD, Dales RE. The role of ipratropium bromide in the emergency management of acute asthma exacerbation: meta-analysis of randomized clinical trials. Ann Emerg Med 1999;34(1): 8–18.
17. Qureshi F, Pestian J, Davis P, Zaritsky A. Effect of nebulized ipratropium on the hospitalization rates of children with asthma. N Engl J Med 1998;339(15):1030–1035.
18. Rodrigo GJ, Rodrigo C. First-line therapy for adult patients with acute asthma receiving a multiple-dose protocol of ipratropium bromide plus albuterol in the emergency department. Am J Respir Crit Care Med 2000;161(6):1862–1868.
19. Rowe BH, Spooner C, Ducharme FM, Bretzlaff JA, Bota GW. Early emergency department treatment of acute asthma with systemic corticosteroids (Cochrane Review). In: The Cochrane Library, 3, 2001. Oxford: Update Software.
20. Manser R, Reid D, Abramson M. Corticosteroids for acute severe asthma in hospitalized patients (Cochrane Review). In: The Cochrane Library, 3, 2001. Oxford: Update Software.
21. Rowe BH, Bretzlaff JA, Bourdon C, Bota GW, Camargo CA Jr. Magnesium sulfate for treating exacerbations of acute asthma in the emergency department (Cochrane Review). In: The Cochrane Library, Issue 3, 2001. Oxford: Update Software.
22. Alter HJ, Koepsell TD, Hilty WM. Intravenous magnesium as an adjunct in acute bronchospasm: a meta-analysis. Ann Emerg Med 2000;36(3):191–197.
23. Edmonds ML, Camargo CA Jr, Pollack CV Jr, Rowe BH. Early use of inhaled corticosteroids in the emergency department treatment of acute asthma (Cochrane Review). In: The Cochrane Library, 3, 2001. Oxford: Update Software.
24. Schuh S, Reisman J, Alshehri M, Dupuis A, Corey M, Arseneault R, et al. A comparison of inhaled fluticasone and oral prednisone for children with severe acute asthma. N Engl J Med 2000;343(10):689–694.
25. CPS. Global initiative for asthma: global strategy for asthma management and prevention. NHLBI/WHO Workshop Report: 95–3659. Bethesda: National Institutes of Health, 1995.
26. Belda J, Parameswaran K, Rowe BH. Addition of intravenous aminophylline to beta2 agonists in adults with acute asthma (Cochrane Review). In: The Cochrane Library, 3, 2001. Oxford: Update Software.
27. Travers AH, Jones AP, Kelly K, Barker S, Camargo CA Jr, Rowe BH. Intravenous beta$_2$ agonists for acute asthma in the emergency department (Cochrane Review). In: The Cochrane Library, 3, 2001. Oxford: Update Software.
28. Rodrigo G, Rodrigo C, Pollack C, Rowe B. Helium-oxygen mixture for nonintubated acute asthma patients (Cochrane Review). In: The Cochrane Library, 3, 2001. Oxford: Update Software.
29. Graham VAL, Milton AF, Knowles GK, Davies RJ. Routine antibiotics in hospital management of acute asthma. Lancet 1982;1(8269): 418–420.
30. Graham V, Lasserson T, Rowe BH. Antibiotics for acute asthma (Cochrane Review). In: The Cochrane Library, 3, 2001. Oxford: Update Software.
31. Rowe BH, Spooner CH, Ducharme FM, Bretzlaff JA, Bota GW. Corticosteroids for preventing relapse following acute exacerbations of asthma (Cochrane Review). In: The Cochrane Library, 3, 2001. Oxford: Update Software.
32. Verbeek PR, Geerts WH. Nontapering versus tapering prednisone in acute exacerbations of asthma: a pilot trial. J Emerg Med 1995;13(5): 715–719.
33. O'Driscoll BR, Karla S, Wilson M, Pickering CAC, Carrol KB, Woodcock AA. Double-blind trial of steroid tapering in acute asthma. Lancet 1993;341(8841):324–327.
34. Rowe BH, Bota GW, Fabris L, Therrien SA, Milner RA, Jacono J. Inhaled budesonide in addition to oral corticosteroids to prevent relapse following discharge from the emergency department: a randomized controlled trial. JAMA 1999;281(22):2119–2126.
35. Rowe BH, Bota GW, Pollack CV, Emond SD, Camargo CA Jr. Management of acute asthma among adults presenting to Canadian versus US Emergency Departments. Ann Emerg Med 1998;32(3 Pt 2):S2–S3.
36. Brenner BE, Chavda KK, Camargo CA Jr. Randomized trial of inhaled flunisolide versus placebo among asthmatic patients discharged from the emergency department. Ann Emerg Med 2000; 36(5):417–426.
37. Camargo CA Jr for the MARC-4 Investigators. Randomized trial of medium-dose fluticasone vs placebo after an emergency department visit for acute asthma. J Allergy Clin Immunol 2000;105(1 Pt 2): S262.
38. Edmonds ML, Camargo CA Jr, Brenner BE, Rowe BH. Inhaled steroids for acute asthma following emergency department discharge (Cochrane Review). In: The Cochrane Library, 3, 2001. Oxford: Update Software.
39. Stephenson BJ, Rowe BH, Haynes RB, Macharia WM, Leon G. Is this patient taking the treatment as prescribed. JAMA 1993;269(21): 2779–2781.
40. Emond SD, Reed CR, Graff LG IV, Clark S, Camargo CA Jr. Asthma education in the emergency department. On behalf of the MARC Investigators. Ann Emerg Med 2000;36(3):204–211.
41. Emond SD, Camargo CA Jr, Nowak RM. 1997 National Asthma Education and Prevention Program Guidelines: a practical summary for emergency physicians. Ann Emerg Med 1998;31(5):579–589.
42. Wilson AJ, Gibson PG, Coughlan J. Long acting beta-agonists versus theophylline for maintenance treatment of asthma (Cochrane Review). In: The Cochrane Library, 3, 2001. Oxford: Update Software.
43. Ducharme FM, Hicks GC. Anti-leukotriene agents compared to inhaled corticosteroids in the management of recurrent and/or chronic asthma (Cochrane Review). In: The Cochrane Library, 3, 2001. Oxford: Update Software.
44. Clark NM, Gotsch A, Rosenstock IR. Patient, professional and public education on behavioral aspects of asthma: a review of strategies for change and needed research. J Asthma 1993;30(4):241–255.
45. Haby MM, Waters E, Robertson CF, Gibson PG, Ducharme FM. Interventions for educating children who have attended the emergency room for asthma (Cochrane Review). In: The Cochrane Library, 3, 2001. Oxford: Update Software.
46. Gibson PG, Coughlan J, Wilson AJ, Hensley MJ, Abramson M, Bauman A, Walters EH. Limited (information only) patient education for adults with asthma (Cochrane Review). In: The Cochrane Library, 3, 2001. Oxford: Update Software.

47. Gibson PG, Coughlan J, Wilson AJ, Abramson M, Bauman A, Hensley MJ, Walters EH. Self-management education and regular practitioner review for adults with asthma (Cochrane Review). In: The Cochrane Library, 3, 2001. Oxford: Update Software.
48. Cates CJ, Jefferson TO, Bara AI, Rowe BH. Vaccines for preventing influenza in people with asthma (Cochrane Review). In: The Cochrane Library, 3, 2001. Oxford: Update Software.
49. Linde K, Jobst K, Panton J. Acupuncture for chronic asthma (Cochrane Review). In: The Cochrane Library, 3, 2001. Oxford: Update Software.
50. Linde K, Jobst KA. Homeopathy for chronic asthma (Cochrane Review). In: The Cochrane Library, 3, 2001. Oxford: Update Software.
51. Woods RK, Thien FCK, Abramson MJ. Dietary marine fatty acids (fish oil) for asthma (Cochrane Review). In: The Cochrane Library, 3, 2001. Oxford: Update Software.
52. Camargo CA Jr, Weiss ST, Zhang S, Willett WC, Speizer FE. Prospective study of body mass index, weight change, and risk of adult-onset asthma in women. Arch Intern Med 1999;159(21): 2582–2588.

Discussion

Ellrodt: There's some evidence in the secondary prevention literature about a messaging effect during acute hospitalization; which is to say, if a patient is hospitalized and then they are sent home on all the right medications—lipid-lowering agents, smoking cessation counseling, etc—they continue on those medications for at least the next year. Is there any such messaging that's been observed in ED visits around asthma care, to your knowledge?

Rowe: Yes. There's some evidence that messaging does occur—"negative" messaging! If inhaled corticosteroids aren't initiated in the ED, when you check them in 3 weeks, only 1% of them have seen their physician and been given inhaled corticosteroids. So, again, our message to physicians in the emergency setting is: Start them on inhaled corticosteroids so that when they return to their family doctor (when their prescription runs out) they'll be able to tell them whether it helped. There is also evidence that I didn't cover in my presentation (because I ran out of time), from Peter Gibson's reviews. Peter Gibson is an Australian pulmonary specialist, and he's done a lot of work on asthma education. At a recent conference, we reviewed asthma education in the context of the emergency setting. Gibson's data would suggest that limited information—just limited, short bursts of education—have no effect.[1] They might have some effect in the emergency setting, but there's only one trial dealing with that setting. But self-management, in addition to an action plan for patients, actually reduces hospitalizations, repeat exacerbations, and a number of other important outcomes.

You want to give them *something* in the emergency department; there's not a lot of evidence on what we should give them, but whatever we give them should be linked back to their primary care provider. That should be part of their care in the ED; probably as important as medications. The acute phase medications are really a key issue, but they are not the "only message." I don't think there's a lot of evidence that in the first 3 weeks we're going to make a difference unless we give them the right medication. But Gibson's work would suggest that you need to continue with more than just limited information-only interventions.[2] I don't know enough about the in-patient work, but I know that Louis Philippe Boulet in Quebec has done a lot of work across the province looking at all in-patients and out-patients, linking them to asthma education in the hospital, and he's achieved very good results, suggesting that relapses and exacerbations are considerably reduced in the next year. Consequently, the hospital visit, like the ED visit, is a real sentinel event for asthma patients. Does that get at what you're thinking?

REFERENCES

1. Gibson PG, Coughlan J, Wilson AJ, Hensley MJ, Abramson M, Bauman A, Walters EH. Limited (information only) patient education programs for adults with asthma (Cochrane review). In: The Cochrane Library, Issue 2, 2001. Oxford: Update Software.
2. Gibson PG, Coughlan J, Wilson AJ, Abramson M, Bauman A, Hensley MJ, Walters EH. Self-management education and regular practitioner review for adults with asthma (Cochrane review). In: The Cochrane Library, Issue 2, 2001. Oxford: Update Software.

Ellrodt: Yes. The other piece that's really important is this: If you *don't* send them home on the right medication—let's say inhaled corticosteroids—they will *never* get on them. And that's exactly what happens in secondary prevention. If you don't send them home on aspirin, β blockers, and/or angiotensin-converting enzyme inhibitors, after a myocardial infarction, they never get on those medications, even though they should. So I think it's a very similar messaging system—messaging to the patient and messaging to the attending physician in the community.

Guyatt: Congratulations on a superb evidence-based presentation. Did I get it right that you were showing differences in outcome on readmissions, except the ipratropium? Is that right? The anticholinergics?

Rowe: Well, the anticholinergics data are not for the out-patient. We don't know after discharge what works as well. Most physicians don't use anticholinergics for out-patient asthma treatment, but for in-ED treatment, it does seem to work.

Guyatt: Yes, in-patient.

Rowe: It showed a benefit for reducing admissions and improving pulmonary functions.

Guyatt: In admissions as well?

Rowe: Yes. Pulmonary function and admissions for anticholinergics are improved.

Guyatt: So you showed reductions in admissions for *all* those positive ones?

Rowe: Correct.

Guyatt: That's great.

Rowe: However, I eliminated intravenous β agonists, aminophylline, and antibiotics, because they really don't show a benefit. The one that did show a sort of equivalence or no clear benefit to one or the other was the very mildly asthmatic patient being sent home, and I think that's an important one for people to understand.

Guyatt: In the analyses in which you separated the mild from the severe asthma, were the magnitudes of the effects statistically different in the mild and severe, or is it just that you looked at it and they appeared different?

Rowe: You're getting at the issue about subgroup analysis in systematic views. This is an a priori decision; these are magnitudes that are statistically and clinically different. We accept subgroups when there are "within" and "between" study differences. In fact, regarding magnesium, there's a study that separates it *within* the study and shows a clear benefit in severely asthmatic patients, and then *between* studies we also see differences. In addition, we search for a large effect, evidence that it makes physiologic sense, and evidence that the subgroup has been shown in the other systematic views.

Guyatt: One of the benefits of a top-quality meta-analysis is that you have a priori hypotheses about *differences* in effect across different groups, and what Brian is telling us is that they started with an a priori hypothesis that the magnitude of the effect may differ between mildly and severely asthmatic patients; however, they found that it not only *appeared* different, but it was *statistically* different between the mildly and severely asthmatic patients. So that's another strength of the review.

Ellrodt: This is just a brief summary. When patients come into your ED with asthma, do you first check the peak expiratory flow, and then decide whether the asthma is mild, moderate, or severe? Do you do that if you're able to?

Rowe: Are you talking about clinical assessment of acute asthma?

Ellrodt: Yes.

Rowe: There's a lot of debate in the pulmonary literature about peak flows versus FEV_1, but the reality is that when people are sick we need a measure that we can follow over time. I don't really care if I get full pulmonary function, spirometry, or peak flow initially. I want some measure in addition to the pulse oximetry, vital signs, and my clinical examination. We've just done a review of our own institution, just like you've done for pneumococcal vaccination. We've got a care plan for asthma, and 87% of patients have a peak flow measurement at presentation. That's better than it was 10 years ago, but it's not ideal.

One of the problems at the emergency triage is that oximetry is not a very sensitive measure of severity. Unfortunately, many asthmatic adults will be able to talk to you and have decent oxygen saturation, but when you measure their peak flow, it's 25% of predicted. I think there's an under-triage of respiratory problems in the emergency department, and an over-triage of other problems, such as chest pain. So I tell all my asthmatics, "Just say you have chest pains," because they'll get seen faster. (Kidding!) They'll get seen; whereas if you come in with asthma you don't really get that sort of urgency. So pulmonary function measures at some stage are important; some places are better than others, and I think your quality control approach really is the way that most emergency departments are trying to deal with a lot of these very common diseases like COPD, asthma, community-acquired pneumonia, chest pain, deep vein thrombosis.

Ellrodt: Thanks, because it looks like that measurement or some assessments vary, that drives a lot of what you do, in terms of what works and what doesn't work, and so you end up with very different treatment plans, based on that assessment, in terms of severity.

Rowe: Yes, that's true. Again, a lot of physical findings don't change, particularly in adults, until the asthma is very severe. So if you can recognize a really severe asthma exacerbation, they're *really* sick. Moreover, you don't really need a pulmonary function measurement in such patients. They are so sick we often don't even attempt to obtain pulmonary function tests, because they can't complete the test. They're less than 100 L/min peak flow. The other issue about peak flow versus FEV_1 is that when our patients are that sick, when they go to end-expiratory phase their airways collapse, they start coughing, and they don't send you any Christmas cards or wine, or anything. They're not thanking you. Whereas you can get peak flow very quickly and it's a measurement in time. It's one part of the continuum of "assessment."

Evidenced-Based Airway Management

Keith Littlewood MD and Charles G Durbin Jr MD FAARC

Introduction
Initial Emergency Airway Management
Ventilator-Associated Pneumonia
Diagnosis of Ventilator-Associated Pneumonia
Evidence-Based Medicine Analyses of Measures Thought to Reduce the Incidence of Ventilator-Associated Pneumonia
Tracheotomy and Ventilator-Associated Pneumonia
Other Management Measures Influencing Ventilator-Associated Pneumonia
Timing of Tracheotomy
Percutaneous Tracheotomy
Summary

The increased polarity of evidenced-based medicine has changed the approach to evaluation of medical interventions and treatments, either placing them on firm scientific foundations or suggesting that evidence is inadequate to strongly support current or innovative practices. Airway management devices and techniques are essential and common components of clinical care. It is the purpose of this review to identify the levels of evidence that support common and novel techniques in airway management. Very few airway management techniques are supported by large, prospective randomized trials. In resuscitation, defibrillation should take priority over airway management. This is supported by animal studies and several reported series of patient experiences and will never be subjected to a prospective randomized trial. Substantial evidence supports the use of noninvasive ventilation, subglottic endotracheal tube secretion removal, changing ventilator circuits no more frequently than every 7 days, and the use of selective digestive decontamination with systemic antibiotics to reduce the incidence of ventilator-associated pneumonia. Little evidence supports using other measures such as elevating the head of the bed to 30% (but this costs nothing and is intrinsically attractive), use of heat and moisture exchangers, kinetic bed therapy, early tracheotomy, or lung secretion removal techniques to reduce ventilator-associated pneumonia. Percutaneous tracheotomy currently can only be recommended over open surgical tracheotomy based on cost, convenience and late stomal complications; it may be associated with a slightly higher morbidity and mortality. *Key words: evidence-based medicine, airway management, ventilation, ventilator-associated pneumonia, VAP, tracheotomy.* [Respir Care 2001;46(12):1392–1405]

Introduction

Airway management devices and strategies have been subjects of discussion and study for many years. Since the

Keith Littlewood MD and Charles G Durbin Jr MD FAARC are affiliated with the Department of Anesthesiology, University of Virginia, Charlottesville, Virginia.

A version of this report was presented by Charles G Durbin Jr MD FAARC at the Respiratory Care Journal Conference, Evidence-Based Medicine in Respiratory Care, April 20–22, 2001, Banff, Alberta, Canada.

Correspondence: Charles G Durbin Jr MD FAARC, Department of Anesthesiology, University of Virginia Health Science, Box 800710, Charlottesville VA 22906-0170. E-mail: CGD8V@virginia.edu.

invention and perfection of the cuffed endotracheal tube (ETT) in the 1950s, it has become the definitive device for airway maintenance. When compared to no airway device or intervention, the outcome using an ETT in apneic patients or those with an obstructed natural airway is obviously improved. Other airway management techniques and devices are usually compared and contrasted to endotracheal intubation with cuffed ETTs. Many of the reported studies of airway devices are based on controlled use of ETTs in the operating room for short periods during surgical procedures. The use of such reports to generalize to other areas, such as the pre-hospital phase of resuscitation or the post-injury phase of intensive care unit (ICU) care, is of questionable validity.

Besides the issue of techniques and devices used in providing acute airway support, studies of prolonged airway management alternatives have been performed. The risks and benefits of prolonged ETT intubation versus the risks of performing and benefits of maintaining a surgical airway have received extensive attention. Recommendations have been considered as to the optimal timing of tracheotomy and the best techniques by which to perform it. The relationship of the artificial airway to various complications, such as accidental extubation and the incidence of ventilator-associated pneumonia (VAP), is of interest to clinicians and has been investigated.

Evidence-based medicine (EBM), as used in this paper, consists of a critical analytical approach to the available scientific data, both published and unpublished, to derive practical guidance to help clinicians choose the best alternatives in a given situation. As such, evidence-based statements or treatment recommendations will have a graded classification identifying the *level of evidence* that supports the statement. Table 1 provides the definitions used in this paper for grading the levels of evidence and EBM recommendations. Where available, references to previously published EBM recommendations and meta-analyses are included.

This paper reviews the published literature in support of EBM recommendations about airway management techniques and devices. The specific areas to be considered are:

1. Initial emergency airway management in critically ill patients
2. Ventilator-associated pneumonia, relationship to airway devices and management techniques
3. Prolonged intubation, use and timing of tracheotomy and
4. Percutaneous versus surgical tracheotomy

Our goal is to detail the level and quality of experimental support that has been published using EBM principles for various recommendations in these general areas relating to artificial airways. There is a wealth of experimental material published addressing intermediate outcomes, but the goal in this paper is to examine the material related to ultimate patient outcome from the systematic use of techniques and equipment. Though a specific device or technique may be useful and effective in a skilled individual's hands under carefully controlled clinical conditions, its use by the wider population of caregivers and in routine (uncontrolled) clinical settings is the focus of this review.

Initial Emergency Airway Management

The "ABCs" (Airway, Breathing, and Circulation) of resuscitation have recently been challenged by confirmation of the hypothesis that the most important intervention (and only contributor to improved survival) is the rapid delivery of electrical defibrillation in patients suffering

Table 1. Levels of Evidence and Grading of Recommendations

Levels of Evidence	
Level I	Large, randomized trials with clear-cut results; low risk of false-positive (α) error or false-negative (β) error. Or a meta-analysis where the lower limit of the confidence interval exceeds the minimum clinically important benefit.
Level II	Small, randomized trials with uncertain results; moderate to high risk of false-positive (α) and/or false-negative (β) error. Or a meta-analysis where the lower limit of the confidence interval overlaps the minimum clinically important benefit.
Level III	Nonrandomized, concurrent cohort comparisons, contemporaneous controls.
Level IV	Nonrandomized, historical cohort comparisons/controls, and expert opinion.
Level V	Case series, uncontrolled studies, and expert opinion.
Grading of Recommendations	
A	Supported by at least one Level I investigation
B	Supported by only one Level I investigation
C	Supported by Level II investigations only
D	Supported by at least one Level III investigation
E	Supported by Level IV or Level V evidence

cardiac arrest and who are in ventricular fibrillation–the most common arrest rhythm. Delay in defibrillation by even 1 minute results in a significant decrement in survival and significant increase in morbidity.

Recommendation. If a defibrillator is immediately available, opening the airway and rescue breathing should be delayed until the cardiac rhythm is identified and defibrillation accomplished. This a *Grade D* recommendation, supported by several Level III reports.[1–6] The implications of this recommendation on expenses and public policy are huge. If the outcome from resuscitation is to be improved, rapid access to defibrillation in any environment must be made available. This requires strategic distribution of (expensive) devices and an adequately trained provider pool willing and able to use them. This is being accomplished in the United States by the widespread deployment of automated external defibrillators. The movement to public access defibrillation has been embraced in areas of increased risk (at public events such as at sport stadiums, at transportation hubs such as airports, and at predictably stressful situations in elderly males such as gambling casinos).

Recommendation. Endotracheal intubation is no better than other airway devices and bag-valve-mask (BVM) ventilation during pre-hospital resuscitation of pediatric patients in need of airway support. This is a *Grade C* recommendation based on a single prospective, randomized study of 830 children < 12 years old and weighing < 40 kg.[7] Airway management including intubation at the scene was provided by 56 emergency medical technicians experienced in adult intubations, following a brief didactic and practical training session directed at managing the pediatric airway. Despite having several years of experience in adult intubation, only about 60% of patients randomized to the intubation group were successfully intubated. When analyzed with respect to intent to treat, there was no difference in survival (which was poor: 30% with BVM vs 26% with ETT) or the quality of survival (neurologic function) overall. The subgroup following submersion showed a trend to higher survival with ETT (33% with BVM vs 47% with ETT), as did the group with multiple trauma (19% with BVM vs 24% with ETT). Use of BVM favored survival in the foreign body aspiration, child abuse, and reactive airway subgroups and reached statistical significance in the pure respiratory arrest subgroup (50% with BVM vs 30% with ETT). The fact that subgroup analysis indicated such wide differences in outcome suggests that there are conditions under which one approach may be favored. However, because of lack of statistical power, no conclusions could be reached about which patients would benefit from one approach over the other.

Caution must be exercised in applying this recommendation to other patient populations or with other trained providers managing the airway. More experienced responders (ie, respiratory therapists and anesthesiologists) should employ their airway skills as the need presents. Nothing in this recommendation suggests a worse patient outcome from ETT placement by a skilled provider; however, repeated unsuccessful attempts at intubation may be a contributing factor to worse outcomes in the intubation group.

New airway devices have been developed for use in the operating room. Some of these devices are making their appearance in emergency airway management scenarios.

Recommendation. The laryngeal mask airway (LMA) should be substituted for other noninvasive devices (BVM, oral pharyngeal airway, nasal pharyngeal airway) during initial emergency airway management in patients with depressed airway reflexes. This a *Grade D* recommendation, as no large-scale, randomized controlled comparative trial in humans has been published.[8–10]

The LMA is a relatively new airway device, developed in Great Britain by Archie Brain.[11] It has been used in the operating room for routine airway management, in patients with difficult airways, and as a portal for blind intubation or fiberoptic ETT placement. The device was designed to bypass the most common causes of manual ventilation failures—the supraglottic soft tissues, including the soft palate and tongue. Initial placement of the device is easy to teach and learn, and placement skill is easily retained.[12,13] In comparison, BVM ventilation is a more difficult technique to master and retain.[14–16] The major impediment to implementing this recommendation is the difficulty in distributing LMAs to the areas of need. In the new Advanced Cardiac Life Support Guidelines, the LMA is suggested as an alternative airway device based on the evidence that it has generally been shown to be "safe," rather than the definitive device and of proven superiority to BVM techniques.[17] A major limitation in the use of the LMA is cost. They are nondisposable and produced in 7 different sizes for use in neonates to large adults. Each LMA costs several hundred dollars and must be disinfected between each patient use. The life span of the LMA is approximately 30–50 uses, but varies widely, depending on how well the user protects the device. The more widely the device is used, the shorter the life-span. A disposable LMA has been developed, but it is only available in adult size, and it has not yet been shown to be as effective as the original design.

As with other noninvasive airway devices, the LMA provides minimal or no protection from pulmonary aspiration. A variation with an esophageal port for gastric evacuation and decompression has been developed, but is not yet widely available or proven effective. Another issue in using the LMA is that it is less effective at delivering high ventilation pressures than is BVM ventilation. The higher pressures needed in patients with poor pulmonary compliance can more effectively be delivered by 2 rescuers using a BVM device. However, neither device is ideal in that situation, as gastric distention and increased risk of

aspiration is routine with BVM ventilation. The cuffed ETT remains the "definitive" airway for supplying artificial ventilation, especially in conditions of reduced pulmonary compliance.

Ventilator-Associated Pneumonia

Interest in VAP relates to its frequent occurrence and probable impact on patient morbidity and mortality.[18,19] In addition, VAP is associated with a longer length of stay and higher hospital costs.[20,21] Taken together, the occurrence of VAP substantially increases the disease burden to critically ill patients and the cost of providing care. Much has been learned about VAP risk factors, and it is hoped that modifications of patient care can reduce the incidence and consequences of this problem. The approaches to prevention have focused on several general areas, which can be classified as:

Mechanical. Relating to the devices used for management of mechanical ventilation (ventilators, circuits, ETTs, humidification devices, and suctioning methods and devices)

General. Relating to nonventilation aspects of patient care (including the effect of patient position, kinetic beds, gastrointestinal management, and the ICU environment)

Pharmacologic. Including empirical and rotating antibiotic strategy, selective digestive decontamination, and inhaled antibiotics

Though the impact of most of the proposed treatment interventions has not been subjected to large, prospective, randomized trials, there have been several recent evidence-based reviews evaluating the effectiveness of some of these interventions in reducing the incidence of VAP.

Diagnosis of Ventilator-Associated Pneumonia

One of the problems in studying VAP has been the difficulty of establishing the diagnosis. Different criteria are often used by different investigators, and comparison of separate studies has been difficult. Though the Centers for Disease Control have general diagnostic guidelines for VAP, many different specific tests are reported in studies. In April 2000 an EBM review of diagnostic tests for VAP was published in a supplement in *Chest*.[22] The presence of a new fever, elevated white blood cell count, and either a new infiltrate on chest radiograph or development of purulent sputum are considered suggestive of VAP.[23] These criteria are sensitive but not specific, as there is inconsistency in clinician evaluation of radiographs for evidence of infiltration.[24] These problems led the consensus report to recommend that additional studies be used to establish the diagnosis of VAP.

Recommendation. Culture techniques should be used for diagnosis of VAP. This is a *Grade B* recommendation based on the level of evidence evaluation classification used in the consensus process (which differs substantially from the classification used in this paper [see Table 1]). (Grade A recommendations were based on direct scientific evidence. Grade B recommendations were based on scientific evidence supplemented by expert opinion. Grade C recommendations were based on expert opinion alone. Grade D recommendations had no definitive evidence or consensus opinion.[22])

Specific recommendations regarding culture techniques include:

1. Gram-stain and culture of endotracheal aspirates may be useful in diagnosing the presence of VAP. This is a *Grade D* recommendation.

2. The presence of antibody coating or elastin fibers is unreliable and should not be used to diagnose VAP. This is a *Grade C* recommendation.

Other diagnostic recommendations include:

1. VAP should be suspected in patients receiving mechanical ventilation for at least 4 days if 2 or more of the following features are present: temperature of $> 38^{\circ}$ C or $< 36^{\circ}$ C; leukopenia or leukocytosis; purulent tracheal secretions; and decreased oxygenation. In the absence of all of those findings, no further investigations are required, and observation only is required. This is a *Grade B* recommendation.

2. If two or more of those abnormalities are present, a chest radiograph should be evaluated. If the findings are normal (or unchanged), other causes of the abnormal clinical findings should be investigated. This is a *Grade C* recommendation.

Antibiotic treatment recommendations that were proposed from the consensus process included culture-directed and empirical choices. Though the level of evidence favoring a specific approach to culture technique is minimal, use of culture results from the variety of available techniques when VAP is likely to be present was endorsed by the expert panel. In general, culture techniques tend to reduce the use of antibiotics over empirical treatment, but there is no strong evidence that this makes a difference in outcome. If the radiograph shows alveolar infiltrates or an air bronchogram sign, or if the radiographic findings have worsened, one of the following 2 management options (quantitative testing or empirical treatment and qualitative testing) should be pursued:

1. Quantitative procedures include nonbronchoscopic techniques (quantitative endotracheal aspiration, blinded bronchial sampling, catheter-based bronchoalveolar lavage, or blinded protected specimen brush) and bronchoscopic techniques (protected specimen brush, bronchoalveolar lavage, or protected bronchoalveolar lavage). Because these tests have similar sensitivities, specificities, positive predictive values, and likelihood ratios, the choice depends on local expertise, experience, availability, and cost factors.

This is a *Grade D* recommendation. Treatment should be based on the results of diagnostic testing.

2. Decisions about empirical therapy should be determined by the patient's clinical stability, the degree of clinical suspicion, and the results of preliminary tests. The selection of appropriate empirical therapy is based on risk factors, local bacterial epidemiology, and resistance patterns, and involves qualitative testing to identify possible pathogens and may include quantitative testing. This is a *Grade D* recommendation. Therapy is adjusted according to culture results or clinical response.

Invasive tests may avoid the use of antibiotics for clinically unimportant organisms. No direct evidence or consensus indicates the superiority of one invasive test over another. This is a *Grade B* recommendation. Support for this approach was reported in a recent study in which withholding antibiotic therapy when invasive tests did not confirm a clinical suspicion of VAP was not associated with the recurrence of VAP or with increased mortality rates.[25]

Substantial gaps exist in the scientific knowledge of the use of all of these culture techniques. Because these diagnostic techniques are not standardized, reported data on sensitivity and specificity differ. Comparison of the results from different studies and medical centers is difficult. Another problem with the available data is that the populations studied have been very heterogeneous, and some studies have used only subsets of patients in order to emphasize specific points. The Appendix summarizes the EBM analysis regarding the blinded culture techniques.

Additional concerns surround the reports of clinical trials of diagnosis and treatment of VAP. Many patients receive antimicrobial agents before testing is performed, making it impossible to interpret test results. Evidence suggests that after recent antibiotic treatment for suspected VAP, the diagnostic thresholds for numbers of organisms in the culture must be decreased to maintain accuracy.[26] In contrast, ongoing antibiotic therapy for a preexisting infectious disease does not seem to affect the diagnostic accuracy of protected specimen brush or bronchoalveolar lavage. Future studies should define patient populations more carefully, particularly with respect to the onset of antimicrobial therapy. It is possible that the variability of application of invasive testing would diminish and the test characteristics would improve if this approach were standardized. A gold standard has not been defined, but should be, since autopsy studies and studies of lung tissue obtained by biopsy are impractical in clinical care. The only randomized prospective clinical trial comparing invasive techniques and noninvasive quantitative techniques in VAP patients found that invasive techniques led to more frequent changes in antibiotic therapy, though this did not change the mortality rate.[27]

Formal outcome research with randomized controlled trials are needed to assess the various diagnostic and antibiotic management strategies commonly employed for VAP. In addition, these trials should include collection of pertinent data to evaluate economic outcomes using cost-benefit, cost-effectiveness, and cost-utility analyses.

Evidence-Based Medicine Analyses of Measures Thought to Reduce the Incidence of Ventilator-Associated Pneumonia

Noninvasive positive pressure ventilation is a safe and effective means of improving gas exchange in many patients with various types of acute respiratory failure. Patients with acute exacerbations of chronic obstructive pulmonary disease and hypercapnic respiratory failure often respond to noninvasive ventilation with decreased need for intubation and reduced mortality.[28,29] Similarly, noninvasive continuous positive airway pressure was effective in some patients with cardiogenic pulmonary edema, particularly those with hypercapnia. In patients with various forms of acute hypoxemic respiratory failure (eg, pneumonia, congestive heart failure, or chest-wall impairment), this therapy slightly decreased the rate of intubation and improved survival, but the effect was not statistically significant.[30] The efficacy of positive pressure ventilation in patients with hypoxemic respiratory failure has also been shown.[31,32] In addition to affecting mortality, noninvasive ventilation reduces the incidence of VAP, probably by maintaining laryngeal competence and decreasing aspiration of infectious secretions.

Recommendation. If clinically appropriate, noninvasive ventilation should be preferentially employed over intubation and mechanical ventilation. This is a *Grade B* recommendation based on several prospective randomized studies that found improved survival and a lower risk of VAP, as mentioned above.

To help prevent VAP, clinicians caring for mechanically ventilated patients should develop and participate in programs aimed at VAP prevention. Such programs are part of a more general effort directed at preventing nosocomial infections, a cornerstone of which is effective hand washing.[33] Two of the most important components of this approach are the presence of a dedicated person or group that takes ownership of the process and a mechanism for tracking rates of nosocomial infection, distribution of surveillance infection data, and development of plans for dealing with improvement. Clinician participation in changes is essential to successfully change outcomes. The success of such an approach is reflected in reduced morbidity, mortality, and costs.

Recommendation. An identified, dedicated person or group should have responsibility for monitoring nosocomial VAP rates. A multi-disciplinary group, including a respiratory therapist, should have authority for oversight of the local processes aimed at preventing nosocomial

infection, including VAP. This is a *Grade B* recommendation.[34,35]

The development of VAP is influenced by many of the mechanical interventions that occur frequently in the critically ill patient. Recent reviews of the presumed etiology of VAP suggest several areas for active research.[36] The use of noninvasive mechanical ventilation to avoid endotracheal intubation is associated with a substantially reduced incidence of VAP. Changing of ventilator circuits was once thought to reduce the infection risk by removing the reservoir of organisms that rapidly accumulate, thus preventing aspiration of that potentially infectious pool.[37] That idea has been discredited by a host of studies suggesting that circuits need never be changed unless they become damaged, visually contaminated, or obviously soiled. In some studies it appears that scheduled, frequent circuit changes may actually increase the incidence of VAP.[38,39] Current Centers for Disease Control guidelines suggest a lengthened time between circuit changes to prevent VAP, the recommendation being that changes occur no more frequently than every 48 hours.[40]

Recommendation. Ventilator circuits need not be changed until they become nonfunctional or grossly contaminated with blood or secretions. Changes more frequently than every 7 days may be associated with increased incidence of VAP. This is a *Grade B* recommendation.

Adequate humidification of inhaled gases is required to maintain mucociliary function during mechanical ventilation. There are a variety of ways to achieve adequate inhaled humidity. Heat and moisture exchangers (HMEs) can be manufactured to serve as bacterial filters. The effect of HMEs on the rate of VAP has been investigated. In a study of 280 patients, comparing daily HME changes to use of a heated-wire circuit, a low VAP rate during prolonged intubation was observed.[41] The HME group's nosocomial VAP rate was 6%, compared to 16% for the heated-wire group, and total ventilator circuit costs (per group) were lower in the HME group. There was no difference (mean ± SD) in duration of ventilation whether the patient did not develop pneumonia or whether the patient developed an early-onset community-acquired pneumonia or a late-onset hospital-acquired pneumonia. However, total ICU days were lower in the HME group. In addition, the incidence of partial ETT occlusion was not significantly different between the groups (8% for the heated-wire group vs 6% for the HME group). The single complete ETT obstruction that occurred in the study was in the heated-wire group.

Recommendation. Heat and moisture exchangers with bacterial filtering capability are an effective strategy to reduce the incidence of VAP, compared to heated-wire circuits and heated humidifiers. This a *Grade D* recommendation.

In addition to the study described above, several other case series have reported either the same or lower VAP incidence with HME (filter) than with heated humidifiers or heated-wire circuits.[42–45] HMEs probably reduce the aspirated pools of contaminated liquid that often collects in the ventilator circuit. However, the appropriate clinical use of these devices, including changing frequencies, has not been definitively determined. They must be used with caution in patients with copious or thick secretions, poor respiratory muscle reserve, or severe airway obstructive disease, as the incidence of ETT occlusion may be higher.[46]

Investigators have suggested that secretions that pool below the larynx and above the inflated ETT cuff may be a source of aspirated contaminated material and proximately contribute to the development of VAP. Endotracheal tubes with a separate lumen above the cuff to suction pooled secretions from the subglottic space are now available (Hi-Lo Evac tube, Mallinckrodt, Pleasanton, California). Use of these tubes with continuous suction is associated with a reduced incidence and later onset of VAP.[47–50] The clinical utility of these specialized ETTs has not been established, but their use may be an effective component to an organized approach to preventing VAP. An illustration of the use of the published studies of this device in everyday clinical care was recently published.[51] A recent EBM analysis estimated that 7 patients requiring prolonged intubation for respiratory failure must receive this tube to prevent 1 case of VAP.[52] These tubes should not be used in place of the other effective strategies and are probably cost-effectively used in patients expected to require at least 5 days of intubation. There appears to be an increased risk of VAP in patients requiring reintubation for respiratory failure following weaning and extubation.[53,54] It is not clear if the same increased risk exists in patients during elective tube changes or if this risk is due to aspiration or other factors occurring during the time the tube is out, prior to reintubation. This issue is important if a clinician is considering reintubation with this specialized tube to reduce VAP in patients intubated for ≥ 5 days. A protocol for obtaining an answer to this question has been proposed.[55]

Closed-system suction catheters have been used to limit circuit violations in patients undergoing prolonged intubation.[56] Their use does not seem to affect the incidence of VAP.[57,58] The selective digestive tract decontamination strategy suggested by Stoutenbeek et al has been subjected to multiple meta-analyses.[59] Most of these have failed to show mortality benefit but have indicated a moderate reduction in VAP.[60–63] A recent update of the Cochrane Database of Systematic Reviews from the Acute Respiratory Infections Group suggests that in intubated patients the use of selective digestive decontamination combined with prophylactic systemic antibiotic treatment is associated with less VAP and lower mortality than is systemic

antibiotic treatment alone. The question of development of microbial resistance was not addressed by that evidence-based review.[64]

Recommendation. Selective digestive decontamination in conjunction with prophylactic systemic antibiotic treatment should be used in high-risk patients to reduce nosocomial infection risk. This is a *Grade C* recommendation based on the results of several EBM reviews.[65–67]

Overall, 33 trials involving 5,727 people were included in the Cochrane review. There was wide variability in the antibiotics used, patient characteristics, and risk of respiratory tract infections and mortality in the control groups. In 16 trials (involving 3,361 patients) that tested a combination of topical and systemic antibiotic, the average rates of respiratory tract infections and deaths in the control group were 36% and 30%, respectively. There was a significant reduction of both respiratory tract infections (odds ratio 0.35, 95% confidence interval [CI] 0.29–0.41) and total mortality (odds ratio 0.80, 95% CI 0.69–0.93) in the treated group. On average, 5 patients needed to be treated to prevent 1 infection and 23 patients to prevent 1 death. In 17 trials (involving 2,366 patients) that tested topical antimicrobial agents alone, the rates of respiratory tract infections and deaths in the control groups were 28% and 26%, respectively. There were significantly fewer respiratory tract infections (odds ratio 0.56, 95% CI 0.46–0.68), but total mortality was not different (odds ratio 1.01, 95% CI 0.84–1.22) in the treated group.

From this review, it can be concluded that a combination of topical and systemic prophylactic antibiotics can reduce respiratory tract infections and overall mortality in adult patients receiving intensive care. The design of the trials included in this systematic review does not allow one to assess whether the treatment leads to antimicrobial resistance.

Semirecumbent positioning of patients receiving mechanical ventilation is suggested as a method of reducing VAP; this effect is presumed to be due to the reduced incidence of aspiration of oral-gastric secretions.[68] One randomized trial of using semirecumbent body positioning in intubated and mechanically ventilated patients found a lower incidence of nosocomial pneumonia.[69] The study was stopped early (after only 90 patients were studied) when interim analysis showed that the semirecumbent position was clearly superior. Fewer patients in the semirecumbent group developed clinically suspected ($p = 0.003$) or microbiologically confirmed ($p = 0.018$) nosocomial pneumonia than in the supine group. The groups did not differ, however, in mortality (18% in the semirecumbent group vs 28% in the supine group, $p = 0.3$). The major difference was seen in patients receiving enteric feeding. Others have shown increased reflux and aspiration of radioactive markers placed in the stomach in patients treated supine compared to semirecumbent.[70,71]

Tracheotomy and Ventilator-Associated Pneumonia

Though there is a belief that tracheotomy may protect against development of VAP, no definitive study has supported that belief. The advantages of tracheotomy include security of the airway, better airway patency, lower resistance to breathing, easier suctioning, increased patient comfort, less laryngeal damage and dysfunction, and more rapid weaning. However, the effect on VAP is undetermined.

Other Management Measures Influencing Ventilator-Associated Pneumonia

Many other airway interventions and management techniques are believed by some to be important in increasing or decreasing the incidence of VAP. Use of continually moving (kinetic) beds has some support. The major impact of these devices is on development of pressure necrosis; however, a positive but moderate impact on pulmonary secretion clearance is suggested. Four studies show a trend toward lower VAP rates in patients receiving kinetic bed treatment.[72–75] In one trial, the VAP rate was significantly reduced, suggesting that 4 patients would need to be nursed on a kinetic bed (rather than a standard bed) to prevent 1 episode of VAP.[75] Patient discomfort but not physiologic instability resulted in the withdrawal of some patients in those trials.

Other suggestions to reduce the incidence of VAP are of unproven efficacy; these include provision of immune-enhancing nutrition, use of oral rather than nasal ETT, prevention of gastric distention, maintenance of adequate ETT cuff pressure, controlled rather than spontaneous ventilation, use of disposable airway devices, inhaled prophylactic antibiotics, and antibiotic rotation. Much remains to be determined about control of this common clinical problem.

Timing of Tracheotomy

Tracheotomy is a frequently-performed airway procedure in the critically ill. The benefits attributed to tracheotomy for long-term airway management are improved patient comfort; increased airway security; lower resistance to gas movement, improved opportunities for eating and speaking; more rapid weaning from mechanical ventilation; lower incidence of VAP; fewer oral, nasal, and laryngeal complications; and better ability to suction lower airway secretions. Though the acute risks of the procedure are well-known, long-term effects, especially when employing newer methods for tracheotomy, are yet to be adequately quantified. In fact, there are very little quality data available establishing the benefits listed above. The decision to perform a tracheotomy for prolonged airway support involves a clinical decision that the risks of per-

forming a tracheotomy outweigh those of continued translaryngeal intubation. Conventionally, patients requiring intubation for > 3 weeks are considered candidates for tracheotomy (this is a *Grade E* recommendation). Because the long-term airway risks of tracheotomy are probably increased by a preceding prolonged translaryngeal intubation, tracheotomy should be performed as soon as the long-term need can be determined.

The presumed safety of an established surgical airway is based on the belief that, should the airway become dislodged or occluded, caregivers with minimal airway skills can easily maintain or replace it. This has led to the practice of early ICU discharge following tracheotomy. This practice saves institutional resources and frees up ICU beds. The beneficial impact on an individual patient is less obvious. Though patency of an established tracheostomy stoma is excellent, at least 7–10 days are required for the stoma to mature. Should the tracheostomy tube become displaced in the first 24–72 hours, successful blind replacement is difficult or impossible. Patient morbidity and mortality are likely should this inadvertent decannulation occur in a place where airway expertise is not immediately available. No data are reported to establish the magnitude of that risk.

Recommendation. Tracheotomy should be considered in any patient expected to require prolonged airway support and who is expected to benefit from its placement. This is a *Grade E* recommendation based entirely on case reports, case series, and uncontrolled comparisons. It is supported by the observations that complications from the procedure appear to be acceptable in adults and that mortality attributable to the procedure is rare. The overall risk of death from all causes in patients subjected to tracheotomy is on the order of 10–30%, justifying the 0.5–2% reported death rate from the procedure.

Recommendation. Tracheotomy should be performed as soon as possible after the need for prolonged intubation can be identified, based on the disease process and patient wishes. This is often within 7 days of onset of respiratory failure and maybe sooner in the neurologically impaired patient.[76–78] This is a *Grade C* recommendation.

The balance between risk and benefit of early tracheotomy is difficult to determine in critically ill patients requiring artificial airway support. Based on an earlier consensus conference, tracheotomy was recommended to be considered around day 10 if intubation could reasonably be expected to be needed for at least 3 weeks.[79] With the advent of safer and more efficient techniques, such as bedside percutaneous dilation tracheotomy, more series with early tracheotomies have been reported. Though the immediate risks of tracheotomy are well established and not overwhelming, the risk of long-term complications from tracheotomy are more difficult to assess. This is because it is not possible to blind investigators to treatment groups, and because the long-term complications from tracheotomy are really from translaryngeal intubation followed by tracheotomy. Because of clinical uncertainty, it is unlikely that a randomized study of tracheotomy without prior translaryngeal intubation (versus either translaryngeal intubation alone or translaryngeal intubation followed by tracheotomy) will ever be performed. The recommendation of early versus later tracheotomy is supported by several studies indicating essentially no difference in relevant outcomes. In a prospective trial that was based on patient treatment grouping by odd-even admission days, Rodriguez et al noted a significantly lower frequency of pneumonia and shorter duration of mechanical ventilation, ICU stay, and hospital length of stay in patients who underwent tracheotomy within 7 days of intubation than in those who underwent tracheotomy later than 10 days.[80] However, this "pseudo-randomization" technique creates potential bias, since the investigator knows at the time of admission which group the patient will enter. This prior knowledge can alter treatment decisions and affect data analysis. A larger study by Sugerman et al failed to confirm the benefits in another group of trauma patients.[81] In that study, randomized groups of patients underwent tracheotomy between days 3 and 5, 10 and 14, or never (continued translaryngeal intubation). There was no difference in any important outcome variable. In the few patients who were seen months following recovery, there was no difference in laryngeal or tracheal complications between treatment groups. Unfortunately, only a small percentage of the enrolled patients actually completed the protocol; thus, from that study no strong conclusions can be drawn.

The available data are inadequate to support any strong recommendation on the appropriate time to perform a tracheotomy. The procedure should be considered by balancing the expected benefits to the individual patient against the known risks. The risks of *not* performing a tracheotomy in patients requiring prolonged intubation have not been systematically investigated and are probably quite substantial.

Percutaneous Tracheotomy

Open surgical tracheotomy (ST) is a time-established procedure. Believed to have been performed in ancient Egypt, ST became an established procedure for upper airway obstruction secondary to a foreign body, trauma, or infection (diphtheria and croup) by the middle of the 19th century. A relatively new, minimally invasive procedure for placement of a tracheostomy tube was described by Cialgia in 1985.[82] The ease and apparent safety of this technique has led to the widespread use of percutaneous dilatational tracheotomy (PT) in critically ill patients. Believed advantages of PT include a smaller skin incision

and less tissue dissection, leading to less tissue trauma. This may lead to less hemorrhage, fewer infections, fewer long-term tracheal problems, and a better cosmetic result. Because the stoma is smaller, the PT tube may be less likely to become accidentally displaced. A major advantage of PT is that it can easily be performed at the bedside, decreasing the risk and cost of patient transportation to the operating room. PT is also less costly because fewer people are involved, less equipment is used, and PT can be performed sooner after the decision to obtain a surgical airway is made. At the bedside, PT consumes none of the often limited operating room resources. Unlike ST, a variety of clinical specialists perform PT.[83,84]

Several studies have looked at the complications and advantages of PT compared to ST,[85–87] but all of those studies suffered from methodological faults. Obviously, blinding is difficult. Only a few studies are randomized and compare bedside ST to PT.[88,89] In general, it appears that the early complications (including minor bleeding, airway loss, and misplacement of the tracheostomy tube) are more common with PT, whereas stomal infection, late bleeding, and scar formation are more frequent with ST. Head-to-head comparisons include only a small number of patients, but cost and efficiency are major advantages of the PT technique.

Serious complications, although rare, may be more common with PT.[90] A recent meta-analysis identified that posterior tracheal wall injury appears to be a PT-specific problem that involves substantial morbidity.[91] Use of bronchoscopy to more accurately identify the position of entry into the airway may also reduce the likelihood of tracheal injury. A large meta-analysis confirmed that PT is a faster procedure (11.7 vs 26.9 min). In that review, a large number of the PT procedures were performed in the ICU, confirming that the procedure can be performed safely at the bedside. In that analysis it was noted that ST has been performed at the bedside since 1962[92] and was done in the ICU in 66% of the cases of ST included in the review during the period between 1985 and 1996. The location of the operation (ICU vs operating room) remains largely a matter of personal choice and institutional resource allocation. As with other reports, the comparison of PT to ST clearly indicates that the frequency of most complications is lower with PT. The comparison with ST data from the distant past may be unfair because of the advances in general medical care and in the design of tracheostomy tubes and cuffs. ST, as with PT, performed during the recent past (1985 to 1996) is associated with lower rates of perioperative complications.

In comparing PT to ST performed during the same time period (1985 to 1996), differences in complication rates are less obvious. This report suggests that perioperative complications are more frequent with PT, whereas postoperative complications still occur more often with ST. Most of the difference is in complications that are classified as minor. The tight fit of the tracheostomy cannula to the surgical tract probably explains the difference in minor postoperative complications favoring the PT technique. Tamponade of small vessels reduces external hemorrhage, and the lesser tissue dissection and exposure in the tracheostomy wound explains the lower rates of wound infections. Therefore, this meta-analysis tends to support claims that PT causes less tissue trauma, wound infection, and bleeding.

Significant differences were seen in operative mortality and cardiopulmonary arrest. It was estimated that 77 patients per 10,000 suffered those consequences while undergoing PT, whereas only 9 patients per 10,000 experienced those outcomes with ST. The effect of the learning curve of a new technique is hypothesized as one of the contributing factors to explain this difference. The technique has a few unique problems, including producing a false passage, posterior tracheal wall injury, pneumothorax, and tracheoesophageal fistulas, all due to the blind nature of the procedure. However, ICU patients, who tend to be included more often in PT reports, probably have inherently higher complication rates. There may be a publication bias toward complications since they are more frequently seen in the small series when beginning a new technique.

Fracture of a tracheal ring is common during PT, but its clinical importance is uncertain. Several modifications to the original technique have been introduced, including a single dilator method (Ciaglia Blue Rhino, Cook Critical Care, Bloomington, Indiana), a cutting dilator method, and a method to pull rather than push the dilator through the trachea (Fantoni Technique[93]). Taken together, the above factors make any recommendations regarding the role of percutaneous tracheotomy a matter of expert opinion. Since several different specialties claim that tracheotomy is in their domain, it is not surprising that opinions differ as to how it should be performed and by whom. Based on the few groups of patients in whom a single service performed both procedures, PT seems to be an acceptable alternative if neck anatomy and clinical stability are satisfactory.

Recommendation. In patients with suitable neck anatomy, percutaneous dilatational tracheotomy performed at the bedside under bronchoscopic control is an acceptable technique for establishing a long-term airway. This is a *Grade D* recommendation when the procedure is performed by an experienced operator. A stronger recommendation awaits further comparative data.

Summary

With regard to airway management, our recommendations are:

1. If a defibrillator is immediately available, opening the airway and rescue breathing should be delayed until the cardiac rhythm is identified and defibrillation accomplished. This a Grade D recommendation.

2. Endotracheal intubation is no better than other airway devices and BVM ventilation during pre-hospital resuscitation of pediatric patients in need of airway support. This is a Grade C recommendation.

3. The LMA should be substituted for other noninvasive devices during initial emergency airway management in patients with depressed airway reflexes. This a Grade D recommendation.

With regard to VAP:

1. If clinically appropriate, noninvasive ventilation should be preferentially employed over intubation and mechanical ventilation. This is a Grade B recommendation.

2. Ventilator circuits should not be changed until they become nonfunctional or grossly contaminated with blood or secretions. Changes more frequently than every 7 days may be associated with increased incidence of VAP. This is a Grade B recommendation.

3. Heat and moisture exchangers with bacterial filtering capability are an effective strategy to reduce the incidence of VAP, compared to heated-wire circuits and heated humidifiers. This a Grade C recommendation.

4. Selective digestive decontamination in conjunction with prophylactic systemic antibiotic treatment should be used in high-risk patients to reduce nosocomial infection risk. This is a Grade C recommendation.

With regard to tracheotomy, our recommendations are:

1. Tracheotomy should be considered in any patient expected to require prolonged airway support and who is expected to benefit from its placement. This is a Grade E recommendation.

2. Tracheotomy should be performed as soon as possible after the need for prolonged intubation is identified. This is a Grade C recommendation.

3. Percutaneous dilatational tracheotomy performed at the bedside under bronchoscopic control is an acceptable technique. This is a Grade D recommendation when the procedure is performed by an experienced operator.

REFERENCES

1. Eisenberg MS, Copass MK, Hallstrom AP, Blake B, Bergner L, Short F, Cobb L. Treatment of out-of-hospital cardiac arrest with rapid defibrillation by emergency medical technicians. N Engl J Med 1980;302(25):1379–1383.
2. Stults KR, Brown DD, Schug VL, Bean JA. Prehospital defibrillation performed by emergency medical technicians in rural communities. N Engl J Med 1984;310(4):219–223.
3. Larsen MP, Eisenberg MS, Cummins RO, Hallstrom AP. Predicting survival from out-of-hospital cardiac arrest: a graphic model. Ann Emerg Med 1993;22(11):1652–1658.
4. O'Rourke MF, Donaldson E, Geddes JS. An airline cardiac arrest program. Circulation 1997;96:2849–2853.
5. Valenzuela TD, Bjerke HS, Clark LL, et al. Rapid defibrillation by nontraditional responders: the Casino Project. Acad Emerg Med 1998; 5:414–415.
6. Stiell IG, Wells GA, Field BJ, Spaite DW, De Maio VJ, Ward R, et al. Improved out-of-hospital cardiac arrest survival through the inexpensive optimization of an existing defibrillation program: OPALS study phase II. Ontario Prehospital Advanced Life Support. JAMA 1999;281(13):1175–1181.
7. Gausche M, Lewis RJ, Stratton SJ, Haynes BE, Gunter CS, Goodrich SM, et al. Effect of out-of-hospital pediatric endotracheal intubation on survival and neurological outcome: a controlled clinical trial. JAMA 2000; 283(6):783–790.
8. Martens P. The use of the laryngeal mask airway by nurses during cardiopulmonary resuscitation: results of a multicentre trial. Anaesthesia 1994;49(1):3–7.
9. Leach A, Alexander CA, Stone B. The laryngeal mask in cardiopulmonary resuscitation in a district general hospital: a preliminary communication. Resuscitation 1993;25(3):245–248.
10. Samarkandi AH, Seraj MA, el Dawlatly A, Mastan M, Bakhamees HB. The role of laryngeal mask airway in cardiopulmonary resuscitation. Resuscitation 1994;28(2):103–106.
11. Brain AI. Historical aspects and future directions. Int Anesthesiol Clin 1998;36(2):1–18.
12. Roberts I, Allsop P, Dickinson M, Curry P, Eastwick-Field P, Eyre G. Airway management training using the laryngeal mask airway: a comparison of two different training programmes. Resuscitation 1997; 33(3):211–214.
13. Rumball CJ, MacDonald D. The PTL, Combitube, laryngeal mask, and oral airway: a randomized prehospital comparative study of ventilatory device effectiveness and cost-effectiveness in 470 cases of cardiorespiratory arrest. Prehosp Emerg Care 1997;1(1):1–10.
14. Jesudian MC, Harrison RR, Keenan RL, Maull KI. Bag-valve-mask ventilation: two rescuers are better than one: preliminary report. Crit Care Med 1985;13(2):122–123.
15. Elling R, Politis J. An evaluation of emergency medical technicians' ability to use manual ventilation devices. Ann Emerg Med 1983; 12(12):765–768.
16. Gabbott DA, Baskett PJ. Management of the airway and ventilation during resuscitation. Br J Anaesth 1997;79(2):159–171.
17. Guidelines 2000 for Cardiopulmonary resuscitation and emergency cardiovascular care. Part 6: Advanced cardiovascular life support: Section 3: Adjuncts for oxygenation, ventilation and airway control. The American Heart Association in collaboration with the International Liaison Committee on Resuscitation. Circulation 2000;102(8 Suppl):I95–I104.
18. Heyland DK, Cook DJ, Griffith L, Keenan SP, Brun-Buisson C. The attributable morbidity and mortality of ventilator-associated pneumonia in the critically ill patient. The Canadian Critical Care Trials Group. Am J Respir Crit Care Med 1999;159(4 Pt 1):1249–1256.
19. Kollef M. Ventilator-associated pneumonia: a multivariate analysis. JAMA 1993;270(16):1965–1970.
20. Fagon JY, Chastre J, Hance AJ, Montravers P, Novara A, Gibert C. Nosocomial pneumonia in ventilated patients: a cohort study evaluating attributable mortality and hospital stay. Am J Med 1993;94(3): 281–288.
21. Boyce J, Potter-Bynoe G, Dziobek L, Solomon SL. Nosocomial pneumonia in Medicare patients: hospital costs and reimbursement patterns under the prospective payment system. Arch Intern Med 1991;151(6):1109–1114.
22. Grossman RF, Fein A. Evidence-based assessment of diagnostic tests for ventilator-associated pneumonia: executive summary. Chest 2000; 117(4 Suppl 2):177S–181S.
23. Fagon JY, Chastre J, Hance AJ, Domart Y, Trouillet JL, Gibert C. Evaluation of clinical judgment in the identification and treatment of

nosocomial pneumonia in ventilated patients. Chest 1993;103(2): 547–553.
24. Winer-Muram HT, Rubin SA, Ellis JV, Jennings SG, Arheart KL, Wunderink RG, et al. Pneumonia, and ARDS in patients receiving mechanical ventilation: diagnostic accuracy of chest radiography. Radiology 1993;188(2):479–485.
25. Bonten MJ, Bergmans DC, Stobberingh EE, van der Geest S, De Leeuw PW, van Tiel FH, Gaillard CA. Implementation of bronchoscopic techniques in the diagnosis of ventilator-associated pneumonia to reduce antibiotic use. Am J Respir Crit Care Med 1997;156(6): 1820–1824.
26. Souweine B, Veber B, Bedos JP, Gachot B, Dombret MC, Regnier B, Wolff M. Diagnostic accuracy of protected specimen brush and bronchoalveolar lavage in nosocomial pneumonia: impact of previous antimicrobial treatments. Crit Care Med 1998;26(2):236–244.
27. Sanchez-Nieto JM, Torres A, Garcia-Cordoba F, El-Ebiary M, Carrillo A, Ruiz J, et al. Impact of invasive and noninvasive quantitative culture sampling on outcome of ventilator-associated pneumonia: a pilot study. Am J Respir Crit Care Med 1998;157(2):371–376.
28. Brochard L, Mancebo J, Wysocki M, Lofaso F, Conti G, Rauss A, et al. Noninvasive ventilation for acute exacerbations of chronic obstructive pulmonary disease. N Engl J Med 1995;333(13):817–822.
29. Meduri GU, Turner RE, Abou-Shala N, Wunderink RG, Tolley E. Noninvasive positive pressure ventilation via face mask: first-line intervention in patients with acute hypercapnic and hypoxemic respiratory failure. Chest 1996;109(1):179–193.
30. Keenan SP, Kernerman PD, Cook DJ, Martin CM, McCormack D, Sibbald WJ. Effect of noninvasive positive pressure ventilation on mortality in patients admitted with acute respiratory failure: a meta-analysis. Crit Care Med 1997;25(10):1685–1692.
31. Wysocki M, Tric L, Wolff MA, Millet H, Herman B. Noninvasive pressure support ventilation in patients with acute respiratory failure: a randomized comparison with conventional therapy. Chest 1995; 107(3):761–768.
32. Antonelli M, Conti G, Rocco M, Bufi M, De Blasi RA, Vivino G, et al. A comparison of noninvasive positive-pressure ventilation and conventional mechanical ventilation in patients with acute respiratory failure. N Engl J Med 1998;339(7):429–435.
33. Doebbeling BN, Stanley GL, Sheetz CT, Pfaller MA, Houston AK, Annis L, et al. Comparative efficacy of alternative hand-washing agents in reducing nosocomial infections in intensive care units. N Engl J Med 1992;327(2):88–93.
34 Kelleghan SI, Salemi C, Padilla S, McCord M, Mermilliod G, Canola T, Becker L. An effective continuous quality improvement approach to the prevention of ventilator-associated pneumonia. Am J Infect Control 1993;21(6):322–330.
35. Gaynes RP, Solomon S. Improving hospital-acquired infection rates: the CDC experience. Jt Comm J Qual Improv 1996;22(7):457–467.
36. Kollef MH. The prevention of ventilator-associated pneumonia. N Engl J Med 1999;340(8):627–634.
37. Craven DE, Goularte TA, Make BJ. Contaminated condensate in mechanical ventilator circuits: a risk factor for nosocomial pneumonia? Am Rev Respir Dis 1984;129(4):625–628.
38. Kollef MH, Shapiro SD, Fraser VJ, Silver P, Murphy DM, Trovillion E, et al. Mechanical ventilation with or without 7-day circuit changes: a randomized controlled trial. Ann Intern Med 1995;123(3):168–174
39. Thompson RE. Incidence of ventilator-associated pneumonia (VAP) with 14-day circuit change in a subacute environment. Respir Care 1996;41(7):601–606.
40. Centers for Disease Control and Prevention. Hospital Infection Control Practices Advisory Committee. Guideline for prevention of nosocomial pneumonia. Respir Care 1994;39(12):1191–1236.
41. Kirton OC, DeHaven B, Morgan J, Morejon O, Civetta J. A prospective, randomized comparison of an in-line heat moisture exchange filter and heated wire humidifiers: rates of ventilator-associated early-onset (community-acquired) or late-onset (hospital-acquired) pneumonia and incidence of endotracheal tube occlusion. Chest 1997;112(4):1055–1059.
42. Kollef MH, Shapiro SD, Boyd V, Silver P, Von Harz B, Trovillion E, Prentice D. A randomized clinical trial comparing an extended-use hygroscopic condenser humidifier with heated-water humidification in mechanically ventilated patients. Chest 1998;113(3):759–767.
43. Martin C, Perrin G, Gevaudan MJ, Saux P, Gouin F. Heat and moisture exchangers and vaporizing humifiers in the intensive care unit. Chest 1990;97(1):144–149.
44. Roustan JP, Kienlen J, Aubas P, Aubas S, du Cailar J. Comparison of hydrophobic heat and moisture exchangers with heated humidifiers during prolonged mechanical ventilation. Intensive Care Med 1992;18(2):97–100.
45. Dreyfuss D, Djedaini K, Gros I, Mier L, Le Bourdelles G, Cohen Y, et al. Mechanical ventilation with heated humidifiers or heat and moisture exchangers: Effects on patient colonization and incidence of nosocomial pneumonia. Am J Respir Crit Care Med 1995;151(4): 986–992.
46. Djedaini K, Billiard M, Mier L, Le Bourdelles G, Brun P, Markowicz P, et al. Changing heat and moisture exchangers every 48 hours rather than 24 hours does not affect their efficacy and the incidence of nosocomial pneumonia. Am J Respir Crit Care Med 1995;152(5 Pt 1):1562–1569.
47. Valles J, Artigas A, Rello J, Bonsoms N, Fontanals D, Blanch L, et al. Continuous aspiration of subglottic secretions in preventing ventilator-associated pneumonia. Ann Intern Med 1995;122(3):179–186.
48. Rello J, Sonora R, Jubert P, Artigas A, Rue M, Valles J. Pneumonia in intubated patients: role of respiratory airway care. Am J Respir Crit Care Med 1996;154(1):111–115.
49. Craven DE, Steger KA. Epidemiology of nosocomial pneumonia: new perspectives on an old disease. Chest 1995;108(2 Suppl):1S–16S.
50. Mahul P, Auboyer C, Jospe R, Ros A, Guerin C, el Khouri Z, et al. Prevention of nosocomial pneumonia in intubated patients: respective role of mechanical subglottic secretions drainage and stress ulcer prophylaxis. Intensive Care Med 1992;18(1):20–25.
51. Cook DJ, Hebert PC, Heyland DK, Guyatt GH, Brun-Buisson C, Marshall JC, et al. How to use an article on therapy or prevention: pneumonia prevention using subglottic secretion drainage. Crit Care Med 1997;25(9):1502–1513.
52. Cook D, De Jonghe B, Brochard L, Brun-Buisson C. Influence of airway management on ventilator-associated pneumonia: evidence from randomized trials. JAMA 1998;279(10):781–787.
53. Mort TC. Unplanned tracheal extubation outside the operating room: a quality improvement audit of hemodynamic and tracheal airway complications associate with emergency tracheal reintubation. Anesth Analg 1998;86(6):1171–1176.
54. Torres A, Gatell JM, Aznar E, el-Ebiary M, Puig de la Bellacasa J, Gonzalez J, et al. Re-intubation increases the risk of nosocomial pneumonia in patients needing mechanical ventilation. Am J Respir Crit Care Med 1995;152(1):137–141.
55. Bryden DC, Lecky F, Moulton C, Little RA. Emergency intubation for acutely ill and injured patients. [Protocol] The Cochrane Library; Date of Most Recent Update: 29–11-2000; Date of Most Recent Substantive Update: 28–10-1998.
56. Johnson KL, Kearney PA, Johnson SB, Niblett JB, MacMillan NL, McClain RE. Closed versus open endotracheal suctioning: costs and physiologic consequences. Crit Care Med 1994;22(4):658–666.

57. Hurni JM, Feihl F, Lazor R, Leuenberger P, Perret C. Safety of combined heat and moisture exchanger filters in long-term mechanical ventilation. Chest 1997;111(3):686–691
58. Deppe SA, Kelly JW, Thoi LL, Chudy JH, Longfield RN, Ducey JP, et al. Incidence of colonization, nosocomial pneumonia, and mortality in critically ill patients using a TrachCare closed-suction system versus an open-suction system: prospective, randomized study. Crit Care Med 1990;18(12):1389–1393.
59. Stoutenbeek CP, van Saene HKF, Miranda DR, Zandstra DF. The effect of selective decontamination of the digestive tract on colonisation and infection rate in multiple trauma patients. Intensive Care Med 1984;10(4):185–192.
60. Vanderbrouk-Grauls CM, Vanderbrouke-Grauls JP. Effect of selective decontamination of the digestive tract on respiratory tract infections and mortality in intensive care unit. Lancet 1991;338(8771): 859–862.
61. Kollef MH. The role of selective digestive tract decontamination on mortality and respiratory tract infections: a meta-analysis. Chest 1994; 105(4):1101–1108.
62. Hurley JC. Prophylaxis with enteral antibiotics in ventilated patients: selective decontamination or selective cross-infection? Antimicrob Agents Chemother 1995;39(4):941–947.
63. Meta-analysis of randomised controlled trials of selective decontamination of the digestive tract. Selective Decontamination of the Digestive Tract Trialists' Collaborative Group. Br Med J 1993; 307(6903):525–532.
64. Liberati A, D'Amico R, Pifferi S, Leonetti C, Torri V, Brazzi L, Tinazzi A. Antibiotics for preventing respiratory tract infections in adults receiving intensive care. Cochrane Database Syst Rev 2000; (4):CD000022.
65. Nathens AB, Marshall JC. Selective decontamination of the digestive tract in surgical patients: a systematic review of the evidence. Arch Surg 1999;134(2):170–176.
66. Bonten MJ, Weinstein RA. Infection control in intensive care units and prevention of ventilator-associated pneumonia. Semin Respir Infect 2000;15(4):327–335.
67. Bonten MJ, Weinstein RA. Infection control in intensive care units and prevention of ventilator-associated pneumonia. Semin Respir Infect 2000;15(4):327–335.
68. Kollef MH. Ventilator-associated pneumonia: a multivariate analysis. JAMA 1993;270(16):1965–1970.
69. Drakulovic MB, Torres A, Bauer TT, Nicholas JM, Nogue S, Ferrer M. Supine body position as a risk factor for nosocomial pneumonia in mechanically ventilated patients: a randomised trial. Lancet. 1999; 354(9193):1851–1858.
70. Orozco-Levi M, Torres A, Ferrer M, Piera C, el-Ebiary M, de la Bellacasa JP, Rodriguez-Roisin R. Semirecumbent position protects from pulmonary aspiration but not completely from gastroesophageal reflux in mechanically ventilated patients. Am J Respir Crit Care Med 1995;152(4 Pt 1):1387–1390.
71. Torres A, Serra-Batlles J, Ros E, Piera C, Puig de la Bellacasa J, Cobos A, et al. Pulmonary aspiration of gastric contents in patients receiving mechanical ventilation: the effect of body position. Ann Intern Med 1992;116(7):540–543.
72. Gentilello L, Thompson DA, Tonnesen AS, Hernandez D, Kapadia AS, Allen SJ, et al. Effect of a rotating bed on the incidence of pulmonary complications in critically ill patients. Crit Care Med 1988;16(8):783–786.
73. Summer WR, Curry P, Haponik EF, Nelson S, Elston R. Continuous mechanical turning of intensive care unit patients shortens length of stay in some diagnostic-related groups. J Crit Care 1989;4:45–53.
74. de Boisblanc BP, Castro M, Everret B, Grender J, Walker CD, Summer WR. Effect of air-supported, continuous postural oscillation on the risk of early ICU pneumonia in nontraumatic critical illness. Chest 1993;103(5):1543–1547.
75. Whiteman K, Nachtmann L, Kramer D, Sereika S, Bierman M. Effects of continuous lateral rotation therapy on pulmonary complications in liver transplant patients. Am J Crit Care 1995;4(2):133–139.
76. Qureshi AI, Suarez JI, Parekh PD, Bhardwaj A. Prediction and timing of tracheostomy in patients with infratentorial lesions requiring mechanical ventilatory support. Crit Care Med 2000;28(5):1383–1387.
77. Lanza DC, Parnes SM, Koltai PJ, Fortune JB. Early complications of airway management in head-injured patients. Laryngoscope 1990; 100(9):958–961.
78. Klingbeil GE. Airway problems in patients with traumatic brain injury. Arch Phys Med Rehabil 1988;69(7):493–495.
79. Plummer AL, Gracey DR. Consensus conference on artificial airways in patients receiving mechanical ventilation. Chest 1989;96(1): 178–180.
80. Rodriguez JL, Sternberg SM, Luchetti FA, Gibbons KJ, Taheri PA, Flint LM. Early tracheostomy for primary airway management in the surgical critical care setting. Surgery 1990;108(4):655–659.
81. Sugerman HJ, Wolfe L, Pasquale MD, Rogers FB, O'Malley KF, Knudson M, et al. Multicenter, randomized, prospective trial of early tracheostomy. J Trauma 1997;43(5):741–747.
82. Ciaglia P, Firsching R, Syniec C. Elective percutaneous dilatational tracheostomy: a new simple bedside procedure—preliminary report. Chest 1985;87(6):715–719.
83. Crofts SL, Alzeer A, McGuire GP, Wong DT, Charles D. A comparison of percutaneous and operative tracheostomies in intensive care patients. Can J Anaesth 1995;42(9):775–779.
84. Friedman Y, Fildes J, Mizock B, Samuel J, Patel S, Appavu S, Roberts R. Comparison of percutaneous and surgical tracheostomies. Chest 1996;110(2):480–485.
85. Heikkinen M, Aarnio P, Hannukainen J. Percutaneous dilational tracheostomy or conventional surgical tracheostomy? Crit Care Med 2000;28(5):1399–1402.
86. Moe KS, Stoeckli SJ, Schmid S, Weymuller EA Jr. Percutaneous tracheostomy: a comprehensive evaluation. Ann Otol Rhinol Laryngol 1999;108(4):384–391.
87. Muttini S, Melloni G, Gemma M, Casati A, Carretta A, Giudici D, et al. [Percutaneous or surgical tracheotomy: prospective, randomized comparison of the incidence of early and late complications.] Minerva Anestesiol 1999;65(7–8):521–527. *Article in Italian*
88. Gysin C, Dulguerov P, Guyot JP, Perneger TV, Abajo B, Chevrolet JC. Percutaneous versus surgical tracheostomy: a double-blind randomized trial. Ann Surg 1999;230(5):708–714.
89. Porter JM, Ivatury RR. Preferred route of tracheostomy: percutaneous versus open at the bedside: a randomized, prospective study in the surgical intensive care unit. Am Surg 1999;65(2):142–146.
90. Bowen CP, Whitney LR, Truwit JD, Durbin CG, Moore MM. Comparison of safety and cost of percutaneous versus surgical tracheostomy. Am Surg 2001;67(1):54–60.
91. Dulguerov P, Gysin C, Perneger TV, Chevrolet JC. Percutaneous or surgical tracheostomy: a meta-analysis. Crit Care Med 1999;27(8): 1617–1625.
92. Roe BB. Bedside tracheostomy. Surg Gynecol Obstet 1962;115:239–241.
93. Westphal K, Byhahn C, Wilke HJ, Lischke V. Percutaneous tracheostomy: a clinical comparison of dilatational (Ciaglia) and translaryngeal (Fantoni) techniques. Anesth Analg 1999;89(4):938–843.

Appendix

Evidence-Based Comparison of Microbial Culture Techniques Used in Diagnosis and Treatment of Ventilator-Associated Pneumonia

As reported by Campbell, 15 studies were identified that evaluated the accuracy of blinded sampling methods.[1] The studies were performed in patients receiving mechanical ventilation in various types of intensive care units. Included were small numbers of patients with community-acquired pneumonia and who required ventilator support, as well as a few immunocompromised patients. These studies investigated 654 episodes of pneumonia, most of which were thought to be pneumonia on a clinical basis. Of the 654 episodes, 321 were identified as pneumonia, using various methods.

Seven studies investigated blinded sampling only in patients with clinical evidence of pneumonia. No control subjects were included, or the study was designed to measure concordance. All of these studies enrolled patients who were clinically identified as having pneumonia. Also, a fiberoptic bronchoscopy (FOB) procedure was performed and lower respiratory tract samples were collected using a protected brush. Bronchoalveolar lavage (BAL) samples were obtained in only a few of these studies. Since these 7 investigations made up a substantial proportion of the available studies, the results of the protected specimen-brushing (PSB) sampling obtained by FOB was selected as the "gold standard." Thus, the methodology is fairly standard, and was followed in all studies. Additionally, recovery of at least one similar organism in sufficient bacterial concentration by both the PSB sampling method and blinded PSB (BPSB) was required for confirmation. In 5 studies, histology data were available in at least some patients, and in several of those, cultures of lung tissue also were obtained. Unless otherwise stated in the report, sensitivity and specificity were determined using only the findings from the lung histology studies. The major limitations of blinded procedures were that most were non-directed and rarely was positioning radiographically verified. The sensitivity and specificity for each study varied and were probably dependent on prior antibiotic treatment, study population, and reference test employed.

The conclusions were:

- There was a lack of standardization in the type of catheter used, position of the catheter, and, in the case of BAL, the volume of fluid instilled.
- The limited number of studies performed to date suggests that the sensitivity of blinded techniques is similar to that of FOB techniques, ranging from 74 to 97% for blinded bronchial sampling (BBS), from 63 to 100% for mini-BAL, and from 58 to 86% for BPSB. The specificity of the blinded techniques is also similar to that of FOB techniques, ranging from 74 to 100% for BBS, from 66 to 96% for mini-BAL, and from 71 to 100% for BPSB.
- Adverse effects of blinded techniques appear to be minimal and, at worst, are similar to those of FOB-directed diagnostic techniques.

1. Campbell GD Jr. Blinded invasive diagnostic procedures in ventilator-associated pneumonia. Chest 2000;117(4 Suppl 2):207S-211S.

(continued)

Appendix
(continued)

Summary of Findings from Reports Used in the Evidence-Based Medicine Analysis Herein

Report	P	B	Population	Tech	Control	Sens	Spec
Gaussorgues P, Piperno D, Bachmann P, Boyer F, Jean G, Gerard M, Leger P, Robert D Comparison of nonbronchoscopic bronchoalveolar lavage to open lung biopsy for the bacteriologic diagnosis of pulmonary infections in mechanically ventilated patients Intensive Care Med 1989;15(2) 94-98	Yes	Yes	NA	mini-BAL	Histology	89	75
Papazian L, Martin C, Albanese J, Saux P, Charrel J, Gouin F Comparison of two methods of bacteriologic sampling of the lower respiratory tract a study in ventilated patients with nosocomial bronchopneumonia Crit Care Med 1989,17(5):461-464	Yes	No	Vent = 20 d, mixed	BBS	Clinical + FOB-PSB	97	100
Rouby JJ, Rossignon MD, Nicolas MH, Martin de Lassale E, Cristin S, Grosset J, Viars P. A prospective study of protected bronchoalveolar lavage in the diagnosis of nosocomial pneumonia. Anesthesiology 1989;71(5):679-685.	Yes	Yes	Vent > 48 h, SICU	mini-BAL	Clinical (control) Histologic (pneumonia)	80	66
Torres A, Puig de la Bellacasa J, Xaubet A, Gonzalez J, Rodriguez-Roisin R, Jimenez de Anta MT, Agusti Vidal A Diagnostic value of quantitative cultures of bronchoalveolar lavage and telescoping plugged catheters in mechanically ventilated patients with bacterial pneumonia Am Rev Respir Dis 1989;140(2):306-310.	Yes	No	Vent > 24 h, mixed ICU	BPSB	Clinical + FOB-PSB	58	85
Pham LH, Brun-Buisson C, Legrand P, Rauss A, Verra F, Brochard L, Lemaire F. Diagnosis of nosocomial pneumonia in mechanically ventilated patients Comparison of a plugged telescoping catheter with the protected specimen brush. Am Rev Respir Dis 1991;143(5 Pt 1):1055-1061.	Yes	No	Vent > 24 h, SICU	BBS	Clinical + FOB-PSB	80	74
Pugin J, Auckenthaler R, Mili N, Janssens JP, Lew PD, Suter PM Diagnosis of ventilator-associated pneumonia by bacteriologic analysis of bronchoscopic and nonbronchoscopic "blind" bronchoalveolar lavage fluid. Am Rev Respir Dis 1991,143(5 Pt 1) 1121-1129	Yes	No	Vent > 72 h, SICU	mini-BAL	-	73	96
Leal-Noval SR, Alfaro-Rodriguez E, Murillo-Cabeza F, Garnacho-Montero J, Rey-Perez J, Munoz-Sanchez MA. Diagnostic value of the blind brush in mechanically ventilated patients with nosocomial pneumonia. Intensive Care Med 1992;18(7):410-414	Yes	No	Vent > 72 h, mixed ICU	BPSB	Clinical + FOB-PSB	71	92
Middleton R, Broughton WA, Kirkpatrick MB. Comparison of four methods for assessing airway bacteriology in intubated, mechanically ventilated patients. Am J Med Sci 1992;304(4):239-245.	Yes	No	Vent = 1–30 d	BPSB	Clinical + FOB-PSB	75	71
Rouby JJ, Martin De Lassale E, Poete P, Nicolas MH, Bodin L, Jarlier V, Le Charpentier Y, Grosset J, Viars P Nosocomial bronchopneumonia in the critically ill. Histologic and bacteriologic aspects. Am Rev Respir Dis 1992;146(4):1059-1066	Yes	No	Vent > 48 h, SICU	mini-BAL	Autopsy histology	70	69
A'Court CH, Garrard CS, Crook D, Bowler I, Conlon C, Peto T, Anderson E. Microbiological lung surveillance in mechanically ventilated patients, using non-directed bronchial lavage and quantitative culture Q J Med 1993,86(10):635-648	Yes	No	Vent > 24 h, mixed ICU	mini-BAL	Clinical	63	92
Jorda R, Parras F, Ibanez J, Reina J, Bergada J, Raurich JM Diagnosis of nosocomial pneumonia in mechanically ventilated patients by the blind protected telescoping catheter Intensive Care Med 1993,19(7):377-382	Yes	No	Vent > 48 h, mixed ICU	BBS	Clinical	74	100
Jorda R, Parras F, Ibanez J, Reina J, Bergada J, Raurich JM Diagnosis of nosocomial pneumonia in mechanically ventilated patients by the blind protected telescoping catheter. Intensive Care Med 1993,19(7):377-382	Yes	No	Vent > 48 h, mixed ICU	BPSB	Clinical	74	100
Papazian L, Martin C, Meric B, Dumon JF, Gouin F. A reappraisal of blind bronchial sampling in the microbiologic diagnosis of nosocomial bronchopneumonia. A comparative study in ventilated patients. Chest 1993;103(1):236-242.	Yes	No	Vent = 29 d, mixed ICU	BBS	Clinical + FOB-PSB	89	100
Kollef MH, Bock KR, Richards RD, Hearns ML. The safety and diagnostic accuracy of minibronchoalveolar lavage in patients with suspected ventilator-associated pneumonia. Ann Intern Med 1995,122(10):743-748.	Yes	No	Vent > 24 h, MICU	mini-BAL	Clinical + FOB-PSB	100	96
Mank PE, Brown WJ. A comparison of bronchoscopic vs blind protected specimen brush sampling in patients with suspected ventilator-associated pneumonia. Chest 1995,108(1):203-207.	Yes	No	Vent > 72 h, MICU	BPSB	Clinical + FOB-PSB	86	85
Papazian L, Thomas P, Garbe L, Guignon I, Thirion X, Charrel J, Bollet C, Fuentes P, Gouin F Bronchoscopic or blind sampling techniques for the diagnosis of ventilator-associated pneumonia Am J Respir Crit Care Med 1995,152(6 Pt 1) 1982-1991.	Yes	Yes	Vent > 72 h, MICU	BBS	Autopsy culture	83	80
Papazian L, Thomas P, Garbe L, Guignon I, Thirion X, Charrel J, Bollet C, Fuentes P, Gouin F Bronchoscopic or blind sampling techniques for the diagnosis of ventilator-associated pneumonia Am J Respir Crit Care Med 1995,152(6 Pt 1) 1982-1991.	Yes	No	Vent > 72 h, MICU	mini-BAL	Autopsy culture	83	80
Papazian L, Thomas P, Garbe L, Guignon I, Thirion X, Charrel J, Bollet C, Fuentes P, Gouin F Bronchoscopic or blind sampling techniques for the diagnosis of ventilator-associated pneumonia Am J Respir Crit Care Med 1995,152(6 Pt 1):1982-1991	Yes	No	Vent > 72 h, MICU	BBS	Autopsy culture	83	80

P = prospective B = blinded Tech = technology used in trial. Sens = sensitivity (%). Spec = specificity (%) Vent = mechanical ventilation time MICU = medical intensive care unit BBS = blinded bronchial sampling SICU = surgical intensive care unit FOB = fiberoptic bronchoscopy PSB = protected specimen-brushing BAL = bronchoalveolar lavage. BPSB = blinded protected-specimen brushing.

Discussion

Rowe: I wonder if you would comment on the issue of rapid-sequence intubation versus non-rapid-sequence intubation techniques in the acute setting? I know there's a lot of great evidence on which to base decisions, and I wonder what your thoughts are regarding that approach?

Durbin: That's not one of the topics I chose to review, so I can't tell you what the literature says, and so this is an off-the-cuff answer. My opinion is that a rapid-sequence intubation is to prevent gastric regurgitation and aspiration during the intubation process. Anesthesiologists have focused on this problem over the years, viewing it as a critical problem in the operating room, where it is routinely used in any patient who hasn't been NPO [nothing per oral] long enough to guarantee gastric emptying, or in patients who have received narcotics. I've seen aspiration events under anesthesia, but they've never been in patients who were believed to be at risk; they've always been at unsuspected times. They've occurred during anesthetic inductions in patients who were not at aspiration risk. I don't think that I've ever seen a patient regurgitate who I thought was likely to do so in my 25 years of experience. Given that, then, regurgitation and aspiration on induction of anesthesia are probably low-risk problems. I think it's probably overestimated as a risk factor. However, aspiration is certainly one problem you don't want to have.

The *real* benefit of a rapid-sequence intubation is creating optimal intubating conditions. With a rapid sequence you use a relaxant drug, succinylcholine, which provides optimal intubating conditions. If you choose any other drug, you have less optimal intubating conditions. In unskilled hands the chance of being successful at intubating is less. Even in skilled hands the chance of intubating is less if any relaxant other than succinylcholine is used. I think neuromuscular blocker-assisted intubation is a reasonable approach for the uncomplicated emergency airway, with or without a full stomach, where you want rapid access to the airway. I think the complications are probably more likely with a long-acting relaxant, because 5–10% of patients will present a difficult or impossible intubation. In that case you'd like to use a relaxant drug that would wear off quickly. I think a rapid sequence intubation should always include succinylcholine.

However, there are complications from its use: triggering malignant hyperthermia, causing rhabdomyolysis, elevating serum potassium, or causing cardiac arrest in some children. Those are very rare—much more rare than not being able to intubate after the relaxant is given. Succinylcholine will improve the intubation success rate by providing total paralysis, and if intubation is still impossible, the patient will return to spontaneous breathing in several minutes. I don't know if that answers your question or not. I think rapid sequence intubation should be in the armamentarium of anyone providing airway support, and the question of what drug to use is the only item up for debate.

Meade: Based on the evidence available, how would you define a patient who's at high risk for ventilator-associated pneumonia—who would be eligible for SDD [selective digestive-tract decontamination], and do you use it in your clinical practice?

Durbin: The criteria are very explicit in the Cochrane database, and it's basically anyone who's going to be intubated and on a ventilator for a week or more. Duration of ventilation is the most important risk factor, so if you can guess ahead of time that they will need prolonged ventilation, then they would benefit from SDD. If they've had major trauma, if they've undergone gastrointestinal surgery with peritoneal soilage or any other risk for prolonged intubation, they should be considered for SDD.

Do I routinely use SDD? The simple answer is "No." The reason is that I'm not the only practitioner in my environment, and the standards are set by others. Do I believe it *should* be done? I think some of the answers to that question are in "What To Do." I believe that this is getting clearer from analysis of the data.

One thing that should be done is that all orifices need topical antibiotic treatment. This should include antifungal treatment, rectal and vaginal. And what's clear from the latest review is that to reduce mortality you *have* to include *systemic* antibiotics. In my practice in surgical patients this is not a problem. They all receive antibiotics of some sort. It's hard *not* to give them antibiotics. Most have other indications for them. So adding topical antibiotics when caring for surgical patients is a very reasonable next step. This is the population—trauma and surgical patients—that Chris Stoutenbeek described in his original studies.[1] He also did one other thing, which wasn't looked at specifically in the Cochrane review: he showed cultural sterility, or at least a substantially reduced bacterial load, in the gastrointestinal tract. This may be one of the most important differentiating end points of the early studies. Whether you actually reduced the bacterial load was not evaluated in some studies, and that may have been why many studies didn't show any advantage to SDD. Chris was very particular about that end point. He cultured the stool, increasing treatment until it was $< 10^4$ CFU/mL. Nowadays, it looks like even less topical treatment, when combined with systemic antibiotics, does improve outcome. I'd like to see SDD adopted, because I think it's inexpensive and now proven effective. The risk of superinfection and resistance was not addressed in the Cochrane review, and it needs to be addressed.

REFERENCE

1. Stoutenbeek CP, van Saene HK, Miranda DR, Zandstra DF. The effect of selective decontamination of the digestive tract on colonisation and infection rate in multiple trauma patients. Intensive Care Med 1984; 10(4):185–192.

MacIntyre: I'm going to follow up with what Maureen [Meade] started, and maybe try to pin you down a little bit harder. You put up 3 Grade B recommendations, which are fairly high recommendations about selective decontamination, subglottic secretion drainage, and filters on HMEs. Those are all big practice changes for a lot of places. Yesterday we heard Gray [Ellrodt] saying that, when you have compelling evidence, it becomes important for us to make sure the community adopts those things. So why are you not more active in getting those 3 practices established as standards in Charlottesville?

Durbin: Well, how do you know I'm not?

MacIntyre: I'm sorry. Maybe I misunderstood your answer. I thought you just told Maureen that this is not something you do because—and I'm probably loosely quoting you—"Others set the standards."

Durbin: Well, I think that development of community standards of practice is a collaborative effort. There must be someone out front waving the flag, but you have to analyze the risks and benefits of a change to the institution, and that analysis also includes a cost-benefit assessment. The issues of practice that I've chosen to give high recommendations to were not apparent to me until I finished the paper last week. There has not been time to initiate change. I'm delighted to see that the evidence supports a high-level recommendation in several areas. And I think it probably is the right thing to go home and lobby for the ones that are easy and inexpensive to achieve at this point. It takes a while to get change to occur. Some of the suggested changes are in place at Virginia and some are not. I think that the criteria for who is at high risk need to be well worked out. You need to develop a program before you can achieve change, and I personally think these are very reasonable changes that can be made to achieve clinical improvements.

I haven't figured out yet how to implement subglottic secretion removal. That's one change I've thought about most. I have personally changed endotracheal tubes to place the needed special device for subglottic secretion drainage. I don't think that is the right way to go, because there's risk involved in changing the tube. On the other hand, I don't think it's reasonable to put the special (expensive) tube in every patient who *might* end up needing it. Therefore, how to select the right patient to put it in initially has been my dilemma for that particular modality.

As far as ventilator-associated pneumonia and HMEs, that *is* our standard of practice; we use HMEs with filters almost universally, so no change is needed. Finally, the last recommendation is the SDD, which is one of the strongest, but I did not have strong enough data to support using SDD until just recently.

Hess: I guess I would challenge the recommendation regarding the use of filters in HMEs to prevent ventilator-associated pneumonia. I know that was part of the meta-analysis that Deb Cook and associates did a few years ago.[1] I think there is some additional evidence now that suggests that that doesn't make a difference. In fact, if we believe something else that you said, which is that the source of the ventilator-associated pneumonia is a result of what comes around the outside of the airway, rather than what's breathed *through* the airway, it's hard for me to believe that that recommendation *should* make a difference. And, as I said, I think there's some newer evidence now that suggests that whether you use active or passive humidification, whether you use heated-wire circuits or nonheated-wire circuits, the type of humidifier you use, and so forth, really doesn't make any difference.

REFERENCE

1. Cook D, De Jonghe B, Brochard L, Brun-Buisson C. Influence of airway management on ventilator-associated pneumonia: evidence from randomized trials. JAMA 1998; 279(10):781–787.

Durbin: Dean, you are right. I have it mislabeled on my slide. In my paper, only the use of SDD and subglottic secretion removal merited Grade B recommendations for prevention of VAP. The data supporting HMEs with filters is at best a Grade D recommendation.

Weaning from Mechanical Ventilation: The Evidence from Clinical Research

Maureen O Meade MD MSc, Gordon H Guyatt MD MSc, and Deborah J Cook MD MSc

Introduction
Methods
Results
  Different Modes for Titrating Mechanical Support
  Spontaneous Breathing Trials
  Weaning Predictors
  Weaning Protocols
Summary
  Different Modes for Titrating Mechanical Support
  Spontaneous Breathing Trials
  Weaning Predictors
  Weaning Protocols

Mechanical ventilation incurs substantial morbidity, mortality, and costs. Both premature extubation and delayed extubation can cause harm. Therefore, weaning that is both expeditious and safe is highly desirable. The purpose of this review is to summarize the literature related to weaning modes, spontaneous breathing trials, weaning predictors, weaning with noninvasive positive pressure ventilation, and weaning protocols. We used 5 computerized databases and a duplicate independent review process to select articles for this review. We included randomized clinical trials evaluating any weaning interventions and nonrandomized trials of weaning predictors, with a focus on studies reporting clinically important outcomes. We abstracted quantitative data using several metrics and pooled results across studies only when our assessment of the patients, interventions, and outcomes indicated that pooling was legitimate. The available clinical research evidence suggests that, for progressive weaning of the level of mechanical support, it may be best to choose modes other than synchronized intermittent mandatory ventilation and it is unreasonable to be dogmatic about the use of other modes. There may also be substantial benefits to early extubation with back-up institution of noninvasive positive pressure ventilation, as needed, though this remains an experimental approach. For trials of spontaneous breathing, low levels of pressure support may hasten extubation. We did not uncover any consistently powerful weaning predictors, suggesting that formal use of predictors in patients being considered for reduction or discontinuation of mechanical support is unlikely to improve patient care. The likely explanation is that clinicians already fully consider information from weaning predictors in choosing patients for trials of reduction or discontinuation of mechanical ventilation. Finally, implementation of respiratory therapist- or nurse-driven protocols may be useful for all phases of weaning, and clinicians should adopt daily assessment for a trial of unassisted breathing as a safe method to reduce the duration of mechanical ventilation. *Key words: evidence-based medicine, mechanical ventilation, weaning, predictors, spontaneous breathing trial, T-piece trial.* [Respir Care 2001;46(12):1408–1415]

Introduction

The vast majority of critically ill patients cared for in an intensive care unit (ICU) setting require mechanical ventilation. A European survey of practices related to mechanical ventilation indicated that approximately 40% of a patient's time on a ventilator is spent in the process of weaning.[1] Meanwhile, the costs of mechanical ventilation are substantial. Clinical costs to patients include the morbidity and mortality of ventilator-associated pneumonia[2] and ventilator-associated lung injury.[3] There are additional costs incurred when patients are mechanically ventilated, including nursing costs, respiratory therapist (RT) costs, and equipment costs. It stands to reason that clinicians should attempt to wean patients from mechanical ventilation as quickly as possible. However, weaning too quickly may result in cardiorespiratory instability, and premature extubation followed by reintubation is associated with higher mortality.[4] Because mechanical ventilation incurs substantial morbidity, mortality, and costs, and because both premature weaning and delayed weaning can cause harm, weaning that is both expeditious and safe is highly desirable. For these reasons, clinicians and clinical investigators alike are interested in an evidence-based approach to weaning from mechanical ventilation.

Recently, 2 independent professional organizations developed mandates to produce clinical guidelines for weaning from mechanical ventilation: the American College of Chest Physicians and the St Louis University School of Nursing. In partnership with those 2 professional bodies, and under contract from the Agency for Health Care Policy and Research, we set out to summarize the clinical research related to weaning from mechanical ventilation. Our research collaboration involved critical care physicians, RTs, nurses, research methodologists, and weaning experts. Detailed results of that work have been published along with weaning recommendations from the American College of Chest Physicians.[5,6] The purpose herein is to present a brief summary of our findings related to weaning modes, spontaneous breathing trials, weaning predictors, weaning with noninvasive positive pressure ventilation (NPPV), and weaning protocols, with an emphasis on the implications for respiratory care.

Maureen O Meade MD MSc, Gordon H Guyatt MD MSc, and Deborah J Cook MD MSc are affiliated with the Department of Medicine and the Department of Clinical Epidemiology and Biostatistics, McMaster University, Hamilton, Ontario, Canada. Maureen O Meade MD MSc and Deborah J Cook MD MSc are also affiliated with the Canadian Institutes for Health Research.

A version of this report was presented by Maureen O Meade MD MSc at the RESPIRATORY CARE Journal Conference, Evidence-Based Medicine in Respiratory Care, April 20–22, 2001, Banff, Alberta, Canada.

Correspondence: Maureen O Meade MD MSc, Department of Clinical Epidemiology and Biostatistics, HSC-2C10, McMaster University Health Sciences Centre, 1200 Main Street West, Hamilton ON L8N 3Z5, Canada. E-mail: meadema@hhsc.ca.

Methods

Previous publications describe the methods of this review.[5] With the assistance of a professional librarian, we searched 5 electronic databases, dating back as far as 1971: MEDLINE, EMBASE, Cumulative Index to Nursing and Allied Health Literature, HEALTHSTAR, and the Cochrane Database of Systematic Reviews.

Two or more individuals, working independently, conducted each step of our protocol for selecting articles for this review, from the initial review of titles and abstracts to the review of all potentially relevant articles. We included (1) randomized clinical trials evaluating weaning practices and (2) nonrandomized trials of weaning predictors, with a focus on studies reporting clinically important outcomes rather than just physiologic data. Our search identified approximately 3,200 citations, of which nearly 1,000 proved, on review of titles and abstracts, to be potentially relevant. One-hundred sixteen articles met our selection criteria, and we include the results of many of those articles herein.

To extract data, we established a 9-member team of intensivists and RTs who, following a period of training, abstracted a variety of details and data related to research methodology, as well as clinical outcomes and some physiologic data. Data abstractors worked in pairs, reviewing the articles independently and then together to resolve disagreements. They coded all data onto a 20-page form that we developed for the purpose of this project, and research staff scanned the data forms into an electronic database.

Our analytic methods were extremely varied, given the variety of study designs included in the entire series of our reviews. We only pooled data quantitatively when it seemed appropriate, based on examination of the populations, the experimental and control interventions in the original studies, visual inspection of study results, and formal tests for heterogeneity among study results.[7] For weaning predictors we calculated likelihood ratios, which are the most informative index that we can use to summarize diagnostic properties or predictive properties in general, and this holds true for weaning predictors.

Results

Different Modes for Titrating Mechanical Support

When mechanically ventilated patients are recovering from acute illness, clinicians generally reduce mechanical support progressively, over time, as patients are increas-

Table 1A. Titrating Mechanical Support: Pressure Support Versus Multiple Daily T-Piece

Outcome	First Author	Results	Pooled Results
Weaning duration	Brochard[9]	−67.2 h (−143, 8.89)	−19.5 h (−109, 69.8)
	Esteban[8]	24.0 h (−41.7, 86.7)	
Extubation failure	Brochard[9]	RR 0.54 (0.26, 1.13)	RR 0.91 (0.32, 2.58)
	Esteban[8]	RR 1.58 (0.68, 3.68)	

Numbers in parentheses are 95% confidence limits.
RR = relative risk

ingly able to take on the work of breathing themselves. There are a number of approaches to consider in the early stage of weaning. Clinicians may perform daily T-piece trials, gradually increasing the duration of the trials to increase the endurance of the patient, and resting the patient by providing full ventilatory support between trials. Alternatively, one may conduct such trials many times during the same day to (theoretically) build up respiratory endurance more quickly. Or one may gradually reduce the amount of pressure support provided during each inspiration so that patients are continually performing most of the work of breathing that they are capable of, without rest. Another possibility is to gradually reduce the rate of mandatory breaths delivered by the ventilator in synchronized intermittent mandatory ventilation (SIMV) mode, so the patient initiates as many of the breaths as he or she is capable of. Least commonly, and most recently, clinicians may extubate relatively early, and then support a patient with NPPV, if necessary, until they no longer require mechanical support. Several randomized trials have compared these various modes for weaning mechanical support.

Esteban et al and Brochard et al both compared the use of pressure support mode to multiple daily T-piece trials.[8,9] In both studies, investigators enrolled patients when they were (1) deemed potentially extubatable by the attending physicians and then (2) failed a 2-hour trial of spontaneous breathing. The 2 studies differed in the way the T-piece method was employed. In the Esteban trial, study participants were extubated as soon as they could tolerate a 2-hour T-piece trial of spontaneous breathing. In that study, patients weaned more quickly and more successfully using the T-piece method than with pressure support (Table 1A). In contrast, in the Brochard trial, depending on how the patient performed on a spontaneous breathing trial prior to enrollment, the patient had to progress through successful trials of 5, 15, 30, and 60 minutes before being eligible for a spontaneous breathing trial of 120 minutes. In that study, patients weaned more quickly and more successfully with pressure support than the T-piece method. Because of the different protocols for T-piece weans in those 2 studies, it may not be appropriate to pool the results of the studies. However, some clinicians argue that there are innumerable ways of conducting T-piece weans, and that there is some value in understanding if T-piece weans perform better in general than pressure support weans. Therefore we present the pooled results in Table 1A. The confidence intervals around the pooled results are consistent with an important difference in favor of either pressure support or multiple daily T-piece weans.

Those 2 studies also compared SIMV and multiple daily T-piece weans (Table 1B).[8,9] The trend observed suggests that SIMV prolongs weaning by 2 days (on average), though there was no major difference in the rate of extubation failure. The pooled results exclude an important difference in favor of SIMV and suggest that multiple daily T-piece weans are superior.

Similarly, both studies compared SIMV and pressure support weaning modes (Table 1C).[8,9] The trend we observed here suggests that patients take longer to wean on SIMV than on pressure support. The pooled data also exclude an important difference in favor of SIMV and suggest that pressure support weans are superior.

Table 1B. Titrating Mechanical Support: Synchronized Intermittent Mandatory Ventilation Versus Multiple Daily T-Piece

Outcome	First Author	Results	Pooled Results
Weaning duration	Brochard[9]	+33.6 h (−54.7, 122)	+43.9 h (−3.17, 91.0)
	Esteban[8]	+48.0 h (−7.65, 104)	
Extubation failure	Brochard[9]	RR 0.98 (0.59, 1.63)	RR 1.13 (0.71, 1.78)
	Esteban[8]	RR 1.66 (0.69, 3.95)	

Numbers in parentheses are 95% confidence limits
RR = relative risk

Table 1C. Titrating Mechanical Support: Pressure Support Versus Synchronized Intermittent Mandatory Ventilation

Outcome	First Author	Results	Pooled Results
Weaning duration	Brochard[9]	−10.1 h (−17.5, −2.65)	−6.40 h (−13.9, 1.12)
	Esteban[5]	−2.40 h (−10.4, 5.63)	—
Extubation failure	Brochard[9]	RR 0.56 (0.27, 1.14)	RR 0.73 (0.43, 1.24)
	Esteban[5]	RR 0.96 (0.47, 1.95)	—

Numbers in parentheses are 95% confidence limits.
RR = relative risk.

What about studies comparing NPPV weaning with pressure support weaning? In 2 studies,[10,11] patients with chronic obstructive pulmonary disease who had failed 2-hour T-piece trials were weaned with pressure support until specific criteria were met. At that point they were randomly assigned to continue the pressure support weaning or to undergo early extubation with supplemental NPPV, as needed. Both groups of investigators observed a large trend toward better survival using NPPV weaning (Table 2). After pooling those studies, we observed dramatically lower (70%) mortality, which almost reached conventional statistical significance. One study observed a very large and statistically significant reduction in the incidence of nosocomial pneumonia with NPPV.[11] Although the point estimate after pooling data across studies is consistent with a substantially lower rate of nosocomial pneumonia, wide confidence intervals (CIs) preclude strong inferences. There was also a trend toward a large reduction in ICU length of stay associated with NPPV.

Spontaneous Breathing Trials

Spontaneous breathing trials are conducted late in the process of weaning, when clinicians are considering extubating a patient but they are uncertain about the patient's ability to sustain breathing without mechanical support. A number of investigators have conducted randomized trials of techniques for spontaneous breathing trials.

Esteban et al compared low-level (7 cm H_2O) pressure support to T-piece for spontaneous breathing trials (Table 3).[12] In spite of the large sample size, event rates (such as the rate of reintubation) were sufficiently low that most of their data were inconclusive (as indicated by the wide CIs). The rate of nonextubation (failing the first spontaneous breathing trial) was lower with pressure support, indicating that patients were extubated earlier with pressure support than with T-piece trial. More importantly, the combined end point of nonextubation plus reintubation, which together reflect the 2 ways extubation may fail, was not different between the 2 groups. Hospital mortality was also similar in the 2 groups. However, the width of the CIs indicates that one cannot rule out the possibility of either method being superior with respect to patient survival.

In a subsequent randomized study (Table 4), the same group of investigators compared a 30-minute T-piece trial to a 2-hour T-piece trial.[13] Again, low event rates rendered the data inconclusive with respect to clinically important outcomes, particularly mortality, and the combined outcome of nonextubations and reintubation.

In those 2 trials, Esteban et al made important efforts to minimize biases that can lead to erroneous results. Patients were randomly assigned to one of 2 study groups, in a

Table 2. Weaning Mechanical Support with Noninvasive Positive Pressure Ventilation

Outcome	First Author	Results	Pooled Results
Mortality	Nava[11]*	RR 0.33 (0.09, 1.25)	RR 0.30 (0.09, 1.02)
	Girault[10]†	RR 0.19 (0.01, 3.66)	—
Nosocomial pneumonia	Nava[11]	RR 0.07 (0.00, 1.11)	RR 0.29 (0.02, 3.88)
	Girault[10]	RR 0.94 (0.11, 8.22)	—
ICU length of stay	Nava[11]	−8.90 d (−14.7, −3.13)	−5.14 d (−12.2, 1.90)
	Girault[10]	−1.71 d (−6.61, 3.19)	—

*Nava study $n = 50$.
RR = relative risk.
Numbers in parentheses are 95% confidence limits.
†Girault study $n = 33$.
ICU = intensive care unit.

Table 3. Spontaneous Breathing Trials: Pressure Support of 7 cm H_2O Versus T-Piece

Outcome	Results (RR)	p
Hospital mortality	1.06 (0.71–1.57)	0.78
Non-extubation	0.64 (0.43–0.94)	0.02
Reintubation	0.99 (0.66–1.49)	0.95
Combined end point (nonextubation + reintubation)	0.82 (0.63–1.05)	0.12

Numbers in parentheses are 95% confidence limits.
RR = relative risk
Based on results reported by Esteban, from 484 patients. (Adapted from Reference 12.)

Table 4. Duration of T-Piece Trials: 30 Minutes vs 2 Hours

Outcome	Results (RR)	p
Hospital mortality	1.21 (0.83–1.75)	0.33
Non-extubation	0.78 (0.51–1.20)	0.26
Reintubation	1.08 (0.63–1.60)	0.98
Combined end point (nonextubation + reintubation)	0.89 (0.67–1.20)	0.45

Numbers in parentheses are 95% confidence limits.
RR = relative risk
Based on results reported by Esteban, from 526 patients. (Adapted from Reference 13.)

concealed fashion, meaning that investigators and caregivers were unaware of the group to which a patient would be randomized before being enrolled in the trial. In both studies, the 2 study groups were similar at the start of the trial with respect to other potentially important determinants of outcome and, though they could not blind clinicians, the investigators did show that the patients in the 2 groups received similar care with respect to other therapies that might influence weaning. Both studies had complete follow-up and investigators conducted an intention-to-treat analysis, which preserves the benefit of randomization.

Some other randomized trials, smaller and also more susceptible to bias, compared other modes for spontaneous breathing trials. Feeley et al ($n = 25$) and Jones et al ($n = 106$) found no difference between low-level continuous positive airway pressure (CPAP) and T-piece trials with respect to patient-important outcomes,[14,15] and Hastings et al ($n = 18$) observed no difference between CPAP plus intermittent mandatory ventilation and CPAP alone for conducting trials of spontaneous breathing.[16]

Weaning Predictors

We identified 70 articles describing a variety of studies investigating weaning parameters in chronic obstructive pulmonary disease, cardiovascular ICU, and general ICU patients. Among those studies there were 462 putative weaning predictors! Weaning predictors that clinicians currently use, and that investigators have studied, include an assortment of demographic characteristics (eg, age, diagnostic categories), subjective signs (eg, diaphoresis, agitation), vital signs and hemodynamic variables (eg, heart rate, blood pressure), lung mechanics (eg, tidal volume, respiratory rate), gas exchange (eg, P_{aO_2}, [arterial partial pressure of oxygen], P_{aCO_2} [arterial partial pressure of carbon dioxide]), and severity of illness measures (eg, biochemical variables, comorbidities, levels of respiratory support, levels of nonrespiratory support). Investigators have tested those variables individually, as composite scores or derivations, and as complex systems. In addition, investigators have tested some of the indicators to predict a variety of outcomes related to weaning, including success in titrating the level of mechanical support, success in spontaneous breathing trials, successful extubation, and others. This report focuses on predictors of successful extubation.

The most frequently studied and one of the more powerful tests that we identified was the rapid shallow breathing index. Nine studies evaluating the rapid shallow breathing index used a threshold of 100 (or 105) for predicting successful extubation in a general ICU population.[17–25] Reported likelihood ratios associated with a rapid shallow breathing index < 100 ranged from 0.61 to 8.99. When we pooled the data across studies, we found that a rapid shallow breathing index < 100 was associated with a likelihood ratio of 1.49 (95% CI 1.11, 1.99), and a rapid shallow breathing index > 100 was associated with a likelihood ratio of 0.39 (95% CI 0.25, 0.62) (Table 5). This means that a rapid shallow breathing index < 100 minimally increases the likelihood of successful extubation. A rapid shallow breathing index > 100 reduces the chance of successful extubation to a somewhat greater extent, but the diagnostic utility remains small. Therefore, this is a statistically significant but only marginally clinically useful predictor of successful extubation. We found no evidence of a threshold effect. In addition, standardizing the rapid shallow breathing index to body weight did not improve the accuracy of prediction.[26,27]

The other more powerful predictors included respiratory rate and inspiratory pressure/maximum inspiratory pressure, where maximum inspiratory pressure is defined as the maximum inspiratory pressure measured in an occluded airway after 20 s, starting from residual volume (see Table 5). The pooled likelihood ratios indicate that a respiratory rate < 38 breaths/min did not improve the probability of successful extubation in the sum of those studies, though a respiratory rate of > 38 breaths/min reduced the probability of successful extubation slightly.[22–24,28–31] A ratio of inspiratory pressure-to-maximum inspiratory pressure < 0.3 appears to modestly increase the likelihood of successful extubation.[32,33] Those 3 variables were among the

Table 5. Weaning Predictors

Predictor	# Studies	# Patients	LR
$f/V_T < 100$	9	885	1.49 (1.11, 1.99)
$f/V_T > 100$	9	885	0.39 (0.25, 0.62)
RR < 38 breaths/min	7	406	1.02 (0.97, 1.07)
RR > 38 breaths/min	7	406	0.59 (0.25, 1.36)
$P_I/P_{Imax} < 0.3$	2	81	2.23 (1.15, 4.34)
$P_I/P_{Imax} > 0.3$	2	81	0.63 (0.36, 1.10)

LR = likelihood ratio for predicting successful extubation
Numbers in parentheses are 95% confidence limits
f = respiratory frequency
V_T = tidal volume
f/V_T = rapid shallow breathing index
RR = respiratory rate
P_I/P_{Imax} = inspiratory pressure divided by maximum inspiratory pressure
A likelihood ratio of 1 means the post-test probability is the same as the pre-test probability and thus the test result is altogether unhelpful. Values of 1–2 increase probability very little that the patient has the condition being tested for, just as values of 1–0.5 lower the probability very little that the patient has the condition being tested for. Values of 2–5 or 0.5–0.2 represent small but potentially important differences in probability. Values of 5–10 or 0.2–0.1 represent moderate differences in probability. Values > 10 and < 0.1 represent large differences in probability.

most powerful predictors of successful extubation that we identified when all studies were considered together.

Weaning Protocols

The most important additional weaning intervention that we reviewed was the use of weaning protocols.

Ely et al enrolled into their study all mechanically ventilated patients in their medical surgical ICU during a defined period.[34] RTs documented a variety of respiratory variables on a daily basis. When patients met specific criteria, they underwent a 2-hour T-piece trial. If during the T-piece trial they met additional criteria, the RTs recommended extubation. The measurements and trials were done in a blinded manner, such that attending physicians did not know which patients were undergoing protocol-directed weaning, unless they received a recommendation to extubate. The investigators observed a large and statistically significant reduction in the rate of successful extubation during the study period. In addition, they observed a statistically significant reduction in the duration of weaning, by 2 days, among the patients weaned according to the study protocol.

Other groups have evaluated protocols versus physician-directed weaning for earlier stages of the weaning process. A study evaluating computerized weaning protocols showed a statistically significant reduction in extubation failures and a strong trend toward shorter weaning duration associated with the use of computerized protocols.[35] Another trial of a nurse- and RT-directed protocol was too small to be conclusive, though the direction of the results was similar to those in the other trials.[36] A similar use of protocols by Marelich et al was associated with a statistically significant 2.5 day reduction in the duration of mechanical ventilation, but there were also associated increases (not statistically significant) in failed extubations and in mortality.[37]

Summary

There is a vast literature on weaning from mechanical ventilation. We have focused on clinical research evidence in the form of randomized trials, where possible, and observational studies for weaning predictors. In spite of the large volume of data available, we can draw relatively few conclusions.

Different Modes for Titrating Mechanical Support

SIMV weans are definitely no better than T-piece or pressure support weans, and are probably worse. Therefore, it is advisable to use modes other than SIMV for titrating the level of mechanical support. Other weaning modes appear to confer no advantage. Trials of early extubation supplemented with NPPV are associated with lower mortality and shorter ICU stays. Ongoing research will confirm or refute these exciting potential benefits. In the meantime, NPPV remains an experimental approach to weaning, which should, ideally, be used in the context of systematic evaluations such as clinical trials.

Spontaneous Breathing Trials

With respect to spontaneous breathing trials, most current randomized trials provide limited information because of the low rate of adverse events and/or insufficient sample size. In general, there is no evidence of large differences between a variety of ventilator modes used for spontaneous breathing trials, including T-piece, low-level pressure support, low-level CPAP, or intermittent mandatory ventilation. Any of these methods of conducting spontaneous breathing trials is acceptable. However, spontaneous breathing trials using low-level pressure support may be superior to T-piece trials with respect to hastening extubation. The results of randomized trials also suggest that, for most patients, there is no appreciable difference between T-piece trials of 30 minutes and those lasting 120 minutes. If patients appear to tolerate such trials very well for 30 minutes, it may be safe to extubate at that time; however, if there is any uncertainty, we recommend continuing the trial for a total of 120 minutes.

Weaning Predictors

Why do most of the predictors for successful extubation appear to perform so poorly? The likely explanation is that

clinicians have already considered the results of the predictors when they choose patients for weaning trials. In essence, this means that the predictive power of the tests is "used up" by the time investigators formally test their properties in patients who clinicians have already decided are candidates for weaning. The bottom line is that many of these tests may perform far better than the sum of the data suggests. Formal use of weaning predictors in patients whom clinicians have already intuitively chosen as weaning candidates is unlikely to improve patient care. Therefore, clinicians should not focus on a specific predictor when weaning patients from mechanical ventilation.

Weaning Protocols

Ely et al's work suggests that physicians are far too conservative in considering patients ready for spontaneous breathing trial and/or extubation.[34] Therefore, weaning protocols implemented during the final stages of weaning, and perhaps all stages of weaning, can reduce the duration of weaning and may reduce the rate of extubation failures. Certainly clinicians should conduct daily assessments for trials of spontaneous breathing, to reduce the duration of mechanical ventilation. However, all protocols are not necessarily efficacious. The most recent study raises concerns about the risk of reintubation and mortality associated with protocols, which may carry a risk of premature extubation.[37]

REFERENCES

1. Esteban A, Alia I, Ibanez J, Benito S, Tobin MJ. Modes of mechanical ventilation and weaning: a national survey of Spanish hospitals. The Spanish Lung Failure Collaborative Group. Chest 1994;106(4): 1188–1193.
2. Vincent J, Bihari D, Suter PM, Bruining HA, White J, Nicolas-Chanoine MH, Wolff M. The prevalence of nosocomial infection in intensive care units in Europe. Results of the European Prevalence of Infection in Intensive Care (EPIC). JAMA 1995;274(8):639–644.
3. Meade MO, Cook DJ, Kernerman P, Bernard G. How to use an article about harm: the relationship between high tidal volumes, ventilating pressures, and ventilator-induced lung injury. Crit Care Med 1997;25(11):1915–1922.
4. Epstein SK. Etiology of extubation failure and the predictive value of the rapid shallow breathing index. Am J Respir Crit Care Med 1995; 152(2):545–549.
5. Criteria for Weaning from Mechanical Ventilation. Summary, Evidence Report/Technology Assessment: Number 23. AHRQ Publication No. 00-E028, June 2000. Agency for Healthcare Research and Quality, Rockville, MD. http://www.ahrq.gov/clinic/mechsumm.htm. Accessed October 8, 2001.
6. Meade MO, Guyatt GH, Sinuff T, Griffith L, Hand L, Toprani G, Cook DJ. Trials comparing alternative weaning modes and discontinuation assessments. Chest (2001, in press).
7. Oxman AD, Cook DJ, Guyatt GH Users' guides to the medical literature. VI. How to use an overview. Evidence-Based Medicine Working Group. JAMA 1994;272(17):1367–1371.
8. Esteban A, Frutos F, Tobin MJ, Alia I, Solsona JF, Valverdu I, et al. A comparison of four methods of weaning patients from mechanical ventilation. Spanish Lung Failure Collaborative Group. N Engl J Med 1995;332(6):345–350.
9. Brochard L, Rauss A, Benito S, Conti G, Mancebo J, Rekik N, et al. Comparison of three methods of gradual withdrawal from ventilatory support during weaning from mechanical ventilation. Am J Respir Crit Care Med 1994;150(4):896–903.
10. Girault C, Daudenthun I, Chevron V, Tamion F, Leroy J, Bonmarchand G. Noninvasive ventilation as a systematic extubation and weaning technique in acute-on-chronic respiratory failure: a prospective, randomized controlled study. Am J Respir Crit Care Med 1999; 160(1):86–92.
11. Nava S, Rubini F, Zanotti E, Ambrosino N, Bruschi C, Vitacca M, et al. Survival and prediction of successful ventilator weaning in COPD patients requiring mechanical ventilation for more than 21 days. Eur Respir J 1994;7(9):1645–1652.
12. Esteban A, Alia I, Gordo F, Fernandez R, Solsona JF, Vallverdu I, et al. Extubation outcome after spontaneous breathing trials with T-tube or pressure support ventilation. The Spanish Lung Failure Collaborative Group. Am J Respir Crit Care Med 1997;156(2 Pt 1):459–465. [published erratum appears in Am J Respir Crit Care Med 1997;156(6):2028]
13. Esteban A, Alia I, Tobin MJ, Gil A, Gordo F, Vallverdu I, et al. Effect of spontaneous breathing trial duration on outcome of attempts to discontinue mechanical ventilation. Spanish Lung Failure Collaborative Group. Am J Respir Crit Care Med 1999;159(2):512–518.
14. Feeley TW, Saumarez R, Klick JM, McNabb TG, Skillman JJ. Positive end-expiratory pressure in weaning patients from controlled ventilation: a prospective randomised trial. Lancet 1975;2(7938): 725–729.
15. Jones DP, Byrne P, Morgan C, Fraser I, Hyland R. Positive end-expiratory pressure vs T- piece: extubation after mechanical ventilation. Chest 1991;100(6):1655–1659.
16. Hastings PR, Bushnell LS, Skillman JJ, Weintraub RM, Hedley-Whyte J. Cardiorespiratory dynamics during weaning with IMV versus spontaneous ventilation in good-risk cardiac-surgery patients. Anesthesiology 1980;53(5):429–431.
17. Lee KH, Hui KP, Chan TB, Tan WC, Lim TK. Rapid shallow breathing (frequency-tidal volume ratio) did not predict extubation outcome. Chest 1994;105(2):540–543.
18. Mergoni M, Costa A, Primavera S, Salvadori A, Saccani A, Zuccoli P. [Assessment of various new predictive parameters of the outcome of mechanical ventilation weaning]. Minerva Anestesiol 1996;62(5): 153–164. (article in Italian)
19. Leitch EA, Moran JL, Grealy B. Weaning and extubation in the intensive care unit: clinical or index-driven approach? Intensive Care Med 1996;22(8):752–759.
20. Epstein SK. Etiology of extubation failure and the predictive value of the rapid shallow breathing index. Am J Respir Crit Care Med 1995; 152(2):545–549.
21. Epstein SK, Ciubotaru RL. Influence of gender and endotracheal tube size on preextubation breathing pattern. Am J Respir Crit Care Med 1996;154(6 Pt 1):1647–1652. [Published erratum appears in Am J Respir Crit Care Med 1997 Jun;155(6):2115]
22. Yang KL, Tobin MJ. A prospective study of indexes predicting the outcome of trials of weaning from mechanical ventilation. N Engl J Med 1991;324(21):1445–1450.
23. Krieger BP, Isber J, Breitenbucher A, Throop G, Ershowsky P. Serial measurements of the rapid-shallow-breathing index as a predictor of weaning outcome in elderly medical patients. Chest 1997;112(4): 1029–1034.
24. Hilbert G, Gruson D, Portel L, Vargas F, Gbikpi-Benissan G, Cardinaud JP. Airway occlusion pressure at 0.1 s ($P_{0.1}$) after extubation:

an early indicator of postextubation hypercapnic respiratory insufficiency. Intensive Care Med 1998;24(12):1277–1282.
25. Afessa B, Hogans L, Murphy R. Predicting 3-day and 7-day outcomes of weaning from mechanical ventilation. Chest 1999;116(2): 456–461.
26. Khan N, Brown A, Venkataraman ST. Predictors of extubation success and failure in mechanically ventilated infants and children. Crit Care Med 1996;24(9):1568–1579.
27. Baumeister BL, el-Khatib M, Smith PG, Blumer JL. Evaluation of predictors of weaning from mechanical ventilation in pediatric patients. Pediatr Pulmonol 1997;24(5):344–352.
28. Kline JL, Zinnecki GL, Antonenko DR, Bander JJ. The use of calculated relative inspiratory effort as a predictor of outcome in mechanical ventilation weaning trials. Respir Care 1987;32(10):870–876.
29. Ochiai R, Shimada M, Takeda J, Iwao Y, Fukushima K. Contribution of rib cage and abdominal movement to ventilation for successful weaning from mechanical ventilation. Acta Anaesthesiol Scand 1993; 37(2):131–136.
30. Tahvanainen J, Salmenpera M, Nikki P. Extubation criteria after weaning from intermittent mandatory ventilation and continuous positive airway pressure. Crit Care Med 1983;11(9):702–707.
31. Engoren M, Buderer NF, Zacharias A, Habib RH. Variables predicting reintubation after cardiac surgical procedures. Ann Thorac Surg 1999;67(3):661–665.
32. Yang KL. Inspiratory pressure/P_{Imax} ratio: a predictive index of weaning outcome. Intensive Care Med 1993;19(4):204–208.
33. el-Khatib MF, Baumeister B, Smith PG, Chatburn RL, Blumer JL. Inspiratory pressure/maximal inspiratory pressure: does it predict successful extubation in critically ill infants and children? Intensive Care Med 1996;22(3):264–268.
34. Ely EW, Baker AM, Dunagan DP, Burke HL, Smith AC, Kelly PT, et al. Effect on the duration of mechanical ventilation of identifying patients capable of breathing spontaneously. N Engl J Med 1996; 335(25):1864–1869.
35. Strickland-JH J, Hasson JH. A computer-controlled ventilator weaning system: a clinical trial. Chest 1993;103(4):1220–1226.
36. Kollef MH, Shapiro SD, Silver P, St Prentice D, Sauer S, Ahrens TS, et al. A randomized, controlled trial of protocol-directed versus physician-directed weaning from mechanical ventilation. Crit Care Med 1997;25(4):567–574.
37. Marelich GP, Murin S, Battistella F, Inciardi J, Vierra T, Roby M. Protocol weaning of mechanical ventilation in medical and surgical patients by respiratory therapists and nurses: effect on weaning time and incidence of ventilator-associated pneumonia. Chest 2000;118(2): 459–467.

Discussion

Durbin: I'm very excited about the use of NPPV as a weaning tool. I noticed the patients were all COPD patients. I think that needs to be emphasized. Also, the question of whether those patients were at the same point in their disease at the time of entry seems to be critical. It was a small group of patients when they were randomized. You reviewed those studies, and I haven't; were you convinced that the same groups of patients were similar at entry? This is important since they were dramatically different in outcome, a fact that surprises me quite a bit.

Meade: I can't recall all of the details, but there were some issues in baseline similarities.

MacIntyre: Maureen, thanks for your summary of a very complex document. You guys did a terrific job on that thing. Just a comment on the 2 large trials that compared so-called weaning modes: the Brochard and the Esteban trials.[1,2] I feel it is critical to realize that those 2 studies did not really compare *modes*, but, rather, specific ways of *using* modes. I find it misleading to say pressure support was compared to SIMV. A *type* of pressure support, a specific *use* of pressure support, was compared to a specific *use* of SIMV. I think it's difficult to make generalizations about a mode from data derived from only one specific way that the particular mode was used. I think this is particularly true in the way the T-pieces were used in the 2 trials.

The Esteban approach was to do a daily spontaneous breathing trial and let it go for up to 2 hours. If it went for 2 hours, they were ready to be extubated. So it was a combination weaning mode, if you will, but it was also, really, a daily assessment of whether the patient could be taken off the ventilator.

In contrast, the Brochard T-piece approach was much more traditional weaning—very short periods at the beginning that got longer as time went by, and it did not mandate daily weaning assessments. If you look at it on day zero when they start the trial, it is possible in the Esteban approach to get extubated that very day if you pass your T-piece trial, but it's *impossible* to get extubated in the Brochard protocol, because you've got to keep dialing up the T-piece trials over the next 24–48 hours before you can finally get to the point where the patient can be extubated. So that's my long-winded way of saying that I'm not sure it's fair to pool those kinds of studies when you have such widely different ways of using the mode.

REFERENCES

1. Brochard L, Rauss A, Benito S, Conti G, Mancebo J, Rekik N, et al. Comparison of 3 methods of gradual withdrawal from ventilatory support during weaning from mechanical ventilation. Am J Respir Crit Care Med 1994;150(4):896–903.
2. Esteban A, Frutos F, Tobin MJ, Alia I, Solsona JF, Valverdu I, et al. A comparison of 4 methods of weaning patients from mechanical ventilation. Spanish Lung Failure Collaborative Group. N Engl J Med 1995; 332(6):345–350.

Meade: I take your criticism, and accept it, particularly for the use of the T-piece weans in the 2 studies; they were different and some folks might have valid reservations about pooling it. For the other modes, it's true that the different studies would

use, for instance, different protocols for weaning SIMV, and might apply different criteria for extubating patients from SIMV. All I can say is that in both studies there were a group of expert pulmonary physiologists who put together what they thought was the best SIMV wean in one study, and equally smart pulmonary physiologists and intensivists put together the other SIMV wean. I think it's reasonable to pool the data, recognizing that one SIMV wean may be a little better than another one.

Durbin: For a point of clarification, I thought that to get into the Brochard study, the candidates had to be screened with a T-piece trial, and in fact 75% of them didn't make it into the weaning trials because they were able to be immediately extubated.

MacIntyre: That was true for both trials.

Durbin: So, in fact, they already failed the daily trial before they entered into the process, so they probably weren't tested that day. They were certainly screened the day before for not being extubatable.

MacIntyre: But on the next day the Esteban trial sort of did it again, whereas in the Brochard trial you couldn't get to that stage for another 24 to 48 hours. So there was an inherent lag built into the Brochard trial.

Pierson:* I just want to support Neil's caution about the virtual inevitability of introducing bias at some conscious or subconscious level. Although I agree that these were very prominent, sophisticated groups designing the studies, it remains true that the study that found the T-piece to be superior came from a group (or at least a senior author) that has long advocated T-piece weaning, and the study that found pressure support to be superior came from a group that had long advocated pressure support weaning. This is not to imply there was any deception or nefarious intent, but to illustrate how *very* difficult it is, with so many variables involved in the set-up of all these different protocols for the different modes, to *truly* level the playing field.

MacIntyre: Just to re-emphasize that, when you're designing these trials, I think bias is going to happen because the approach you are most comfortable with is almost always going to be the one you're most aggressive with. In contrast, the modes and strategies that you're less comfortable with will lead to a management strategy that is a little more cautious and a little less aggressive. I think that's what happened in those 2 trials.

Rubenfeld: Two comments. First, the issue with Wes Ely's study:[1] I think an important and sometimes overlooked part of the intervention was a direct contact by the respiratory therapist to the physician. I think it was, in part, a time-sensitive reminder, if you will, sort of built into that, as opposed to, you know, I think we get it confused with protocol-based weaning, when in fact, an important part was a timely reminder.

The other is a more general issue that has come up now in a number of our conversations about pooling. We all felt pretty comfortable yesterday with pooling drug studies, and this is why we're so jealous of the cardiologists, and even of the asthma drugs. We're sort of OK with pooling drugs when there can be double blinding, multiple blinding, and it's a drug dose, and we're pretty clear that the only difference between these might be, say, the dosing or the potential for co-interventions. But when we're testing these complicated protocols—the weaning protocol, or the lung-protective ventilation protocols, or the proning protocol—where we're not even sure which aspect is the dose or which of the important co-variates might be the thing, it seems much more difficult to decide when pooling is OK. Do you see what I'm getting at: the complexities of synthesizing studies that are studies of complicated protocols rather than studies of drugs?

*David J Pierson MD FAARC, Division of Pulmonary and Critical Care Medicine, Department of Medicine, University of Washington, Seattle, Washington.

REFERENCE

1. Ely EW, Baker AM, Dunagan DP, Burke HL, Smith AC, Kelly PT, et al. Effect on the duration of mechanical ventilation of identifying patients capable of breathing spontaneously. N Engl J Med 1996;335(25): 1864–1869.

Guyatt: I think that's a good point. The question is what are the alternatives? I would say that although one could have reservations about pooling, pooling is liable to be informative. In other words, if results are all in the same direction and pooling results in an unequivocal effect with a narrow confidence interval, you are on *considerably* stronger ground than if you are left with wide pooling confidence intervals that include no effect. In the latter situation, we have to stop and think very carefully about what is going on, particularly when studies are stopped early, which I think is another concern. So I would agree with your reservations. On the other hand, I would still argue that pooling can be useful with the appropriate approach and a priori hypotheses looking at the differences.

Rubenfeld: I didn't intend my comment to mean that it was a bad idea. It just seemed to me to raise other issues. Again, it's another place where what the EBM consumers want is this kind of black-and-white response, which I think is clear. It just seems that when we pool drug studies from a physiologic basis, people just seem to be more comfortable with it. But as you start to pool these protocols, if the

pooling doesn't show what you want it to show, there is a tendency to say, for instance, that it was the type of protocol or that it was the number of hours in prone position.

Guyatt: That's a great point, but the opportunistic interpretation can be applied to the drug studies as well. If you look at tPA [tissue plasminogen activator] versus streptokinase, for instance, you find no difference. And there are prominent people who believe that that's the appropriate interpretation of the results. But because one of the studies just reached statistical significance with accelerated tPA, that's the one that the company has successfully managed to persuade people is the one that they should believe, and to reject the pooling. So if you have a little bit of difference, a little different way of administering the drug, exactly the same issues start to get introduced into meta-analysis of drugs.

Hess: Some of these trials have been criticized because of what some have called high levels of reintubation. Do you have any sense from reviewing the literature, what is a reasonable reintubation rate? The Esteban studies, for example, have been criticized by some as having high reintubation rates.[1,2]

REFERENCES

1. Esteban A, Alia I, Gordo F, Fernandez R, Solsona JF, Vallverdu I, et al. Extubation outcome after spontaneous breathing trials with T-tube or pressure support ventilation. The Spanish Lung Failure Collaborative Group. Am J Respir Crit Care Med 1997; 156(2 Pt 1):459–465.
2. Esteban A, Frutos F, Tobin MJ, Alia I, Solsona JF, Valverdu I, et al. A comparison of 4 methods of weaning patients from mechanical ventilation. Spanish Lung Failure Collaborative Group. N Engl J Med 1995; 332(6):345–350.

Meade: The rates of reintubation certainly differed across the studies. And there are a number of different types of studies that we evaluated. I can't give you exact values, but I'd say reintubation rates ranged in some studies of spontaneous breathing trials from approximately 5% to 30%. I certainly cannot tell you what is a reasonable reintubation rate. That's something that would be a very important area of research, because until we can standardize physicians' thresholds for instituting the spontaneous breathing trial tests, or thresholds for extubation, then all of this research results in relatively uninformative data.

Evidence-Based Medicine and Sleep Apnea

Steven J Heitman MD and W Ward Flemons MD

Introduction
Why Should Obstructive Sleep Apnea Be Diagnosed and Treated?
Mortality
Morbidity
How Should Obstructive Sleep Apnea Be Diagnosed?
Issue of Resources
Polysomnography and Recommendations from the American Academy of Sleep Medicine Task Force
Alternative Modes of Diagnosis
How Should Obstructive Sleep Apnea Be Treated?
Weight Loss
Mandibular Advancement
Continuous Positive Airway Pressure
Surgery
Summary

There is an increasing body of evidence that obstructive sleep apnea (OSA) affects systemic blood pressure and quality of life. The evidence linking OSA with other types of cardiovascular morbidity and mortality is not as strong. We review the current literature on the health impact, diagnosis, and treatment of OSA and provide a framework for evaluating levels of evidence in each of these areas, with the focus on high quality studies. Clinical prediction rules and unattended portable monitoring devices, such as digital oximeters, are inexpensive and have clinically useful likelihood ratios, sensitivity, and specificity, so they can be considered clinically useful in the evaluation of individuals suspected of having OSA. This approach has the potential to change the probability of disease in some patients to a level at which polysomnography is unnecessary. Recent randomized, placebo-controlled trials have indicated that treating OSA with continuous positive airway pressure improves quality of life, driving simulator performance, blood pressure, and sleepiness. The evidence in support of mandibular advancement is less strong, and surgical measures should be viewed as an option only after continuous positive airway pressure and mandibular advancement have been considered, given the paucity of evidence to support surgery. The quality of research done on the prognosis, diagnosis, and treatment of OSA has improved substantially in recent years. However, there remains a need for additional studies that evaluate ambulatory monitors and for larger randomized controlled trials of therapy with longer patient follow-up to verify the range of benefits that OSA patients can expect from the various treatment modalities. *Key words: evidence-based medicine, obstructive sleep apnea, OSA.* [Respir Care 2001;46(12):1418–1432]

Steven J Heitman MD and W Ward Flemons MD are affiliated with the Department of Medicine, Foothills Medical Centre, University of Calgary, Calgary, Alberta, Canada.

A version of this report was presented by W Ward Flemons MD at the RESPIRATORY CARE Journal Conference, Evidence-Based Medicine in Respiratory Care, April 20–22, 2001, Banff, Alberta, Canada.

Correspondence: W Ward Flemons MD, Department of Medicine, Foothills Medical Centre, University of Calgary, 1403 29th Street, Calgary, Alberta, Canada T2N 2T9.

Introduction

Obstructive sleep apnea (OSA) is a disorder of breathing during sleep. It is characterized by periods of breathing cessation (apnea) and periods of reduced breathing (hypopnea). Apnea and hypopnea have similar pathophysiology and are generally considered equal with respect to their impact on the patient.[1] These breathing disturbances are caused by collapse of the upper airway secondary to relaxation of the pharyngeal dilating muscles. When this occurs, the patency of the upper airway cannot be defended against the suction pressures created by the respiratory muscles during inspiration. In most instances the obstructive event is terminated by an arousal from sleep, lasting only seconds, which the patient is almost never aware of. The arousal is usually associated with a marked increase in sympathetic tone and a surge in blood pressure. Apneas and hypopneas may be accompanied by decreases in oxygen saturation of 20–40 mm Hg in extreme cases; in mild cases the decrease in oxygen saturation may only be trivial. Physiologically, the severity of the disease is most often characterized by the number of breathing disturbances (apneas + hypopneas) per hour of sleep, termed the apnea-hypopnea index (AHI). In addition to the recurrent breathing disturbances during sleep, OSA is characterized by oxygen desaturations, brief arousals, sleep fragmentation, and increased nocturnal blood pressure. OSA patients are often loud snorers, and snoring is thought to be a useful marker of the disease. Patients frequently complain of unrefreshing sleep, excessive daytime sleepiness, and impairment in cognitive tasks such as concentration and memory.

There is debate whether OSA is associated with increased morbidity and mortality. The current evidence is largely based on retrospective and cross-sectional studies, which because of their design cannot prove causality. A growing body of evidence supports the diagnosis and treatment of OSA because effective therapies are available that can reverse the disorder and often result in improved quality of life. Nevertheless, the conclusions that can be drawn from the current body of literature are limited because there is a paucity of well-conducted randomized controlled trials.

Despite growing acceptance that treating OSA may improve morbidity and quality of life, the majority of patients are not diagnosed or treated. This is in part due to the fact that most health care professionals do not include a sleep assessment in taking a medical history, but also because the health care costs of diagnosing and treating OSA are substantial. Polysomnography, the reference standard test for diagnosing OSA, is expensive and labor intensive, which limits its widespread use. As a result, efforts have been made toward developing less expensive, yet equally effective, case finding strategies that can be used more widely.

Treatment of OSA can include weight loss, oral appliances, and continuous positive airway pressure (CPAP). Surgical interventions are also available, but are generally reserved for those who have failed these other less invasive therapies. CPAP is the most effective method of treating OSA, but low compliance remains a factor with many patients who try it.

Decisions surrounding the management of OSA patients depend on being able to address 3 fundamental questions:

1. What are the risks to OSA patients if left untreated (prognosis)?
2. What evidence is there that treatment modifies those risks?
3. Assuming that there are modifiable risks, what is the best way to diagnose OSA?

Why Should Obstructive Sleep Apnea Be Diagnosed and Treated?

A medical disorder is important to diagnose and treat if it increases the risk of early mortality or excess morbidity or reduces quality of life when left untreated.[2] Additionally, it is important that the treatments have been shown to do more good than harm, thus resulting in a positive effect on mortality, morbidity, or quality of life. OSA is a disorder that has only recently been described and is in many respects in its infancy with respect to recognizing the impact it has on patients. For clinicians who have followed OSA patients for years and have witnessed patients having repeated apneas accompanied by alarming degrees of oxygen desaturation, the issues of potential harm to patients and benefit from treatment seem obvious. As a result, many feel that large clinical trials are not needed. However, given the lack of well designed clinical trials to date, it has become a challenge for clinical sleep medicine researchers to demonstrate to other clinicians, epidemiologists, and health care administrators the impact of this disorder on the general population.

It is known from large-scale epidemiological studies that a large proportion of the general population experiences breathing disturbances during sleep. The estimated prevalence depends on the definition of OSA that is used. One of the challenges in this field is determining the AHI that should be used to define clinically important OSA. If a level of 5 is used, then 24% of males and 9% of females (age 30–60) have been shown to meet criteria for OSA.[3] Since the major manifestation of OSA is excessive daytime somnolence, this has become the major defining criterion of the OSA syndrome. The prevalence of OSA syndrome in that same population is 4% of males and 2% of females.[3]

Published reports link OSA to a number of adverse health outcomes, including systemic hypertension, stroke, myocardial infarction, cardiac arrhythmias, motor vehicle

accidents, and mortality. It is possible that OSA is causal or merely a marker of another condition that is the true cause of morbidity and mortality. For example, a population of OSA patients may be found to have a higher prevalence of myocardial infarction than a control group without OSA. However, it is possible that the OSA patients are more obese and have higher blood pressures than the controls, thus implicating systemic hypertension as the causal factor for the higher myocardial infarction rate.

For a disorder such as OSA to be linked to these types of adverse outcomes, it is critical to look at the quality of the evidence. The most conclusive type of study to show causality is a randomized trial in which a cohort of patients is randomized to receive either no treatment or treatment that completely reverses the condition. The 2 groups should be large enough so that potentially confounding factors such as hypertension, obesity, smoking status, and diabetes are equally distributed among them. When the groups are followed over time it can be determined if the untreated group has a statistically higher incidence of adverse outcomes, in which case a causal relationship could be inferred. This type of study would probably not be ethical and has never been done.

In the absence of this type of study, the next best type of evidence is a cohort study: a group of subjects representative of the general population that is followed over time to see what type of adverse outcomes they develop. Participants in clinical trials may also be followed over time; however, they are often not representative of the general population and thus the findings of such studies may not be generalizable. It is also possible to collect cases of individuals who already have an adverse outcome (eg, myocardial infarction) and compare them with a series of controls that do not have the adverse outcome. In these "case-control" studies both the cases and the control groups are analyzed for the prevalence of a prognostic factor (eg, sleep apnea). This type of study is problematic because there is potential for bias in the selection of cases and controls and because known confounding factors may not be adequately controlled. Even if the study design is rigorous and all known confounding factors are controlled, there may still be other unsuspected factors that are not taken into account, thus leading to erroneous conclusions about causality.

A number of questions have been suggested to evaluate the validity of published studies that report results on prognosis. The questions have been separated into primary and secondary guides[4,5] (Table 1).

Table 1. Guides and Grading System for Evidence About Prognosis of Sleep Apnea

Primary Guides*
1. Was there a representative and well-defined sample of patients who were at similar points in the course of the disease?
2. Was follow-up sufficiently long and complete?

Secondary Guides*
1. Were objective and unbiased outcome criteria used?
2. Was there adjustment for important prognostic factors?

Evidence Grading System† (quality of evidence in studies reporting data on prognosis)
- Level 1a. A systematic review of studies (all of which showed consistently similar results) that used an inception cohort (prospective studies)
- Level 1b. An individual study of an inception cohort with ≥ 80% follow-up
- Level 2a. A systematic review of either retrospective cohort studies or untreated control groups in a randomized controlled trial (all of which showed consistently similar results)
- Level 2b. A retrospective cohort study or an untreated control group in a randomized controlled trial
- Level 3. No methodology specified
- Level 4. Case series and poor quality prognostic cohort studies
- Level 5. Expert opinion without explicit critical appraisal

*Adapted from Reference 4
†Adapted from Reference 5

Mortality

In 1997 Wright et al[6] systematically reviewed the literature on the health effects of sleep apnea. There were 6 studies that examined the possible impact of OSA on mortality. Three of the studies were prospective cohorts of elderly subjects, many with substantial comorbidity. The results did not indicate a consistent relationship to mortality, especially when controlled for comorbid illness. Of the 3 studies in younger subjects, one had no control group and the second showed no difference in all-cause mortality between the OSA and control groups. The third failed to report the duration of follow-up, used self-reported data on death, and failed to control for pre-existing morbidity or other potential confounders such as body-mass index. Therefore the data on mortality is of low quality (Level 4 evidence) and shows conflicting results. Thus, at this time it is not possible to justify recommending treatment for OSA on the basis of reducing mortality.

Morbidity

Cardiovascular Disease. When the same authors[6] critically reviewed the association of OSA and heart disease (arrhythmias, cardiac ischemia, left ventricular hypertrophy), similar conclusions were reached. Studies that looked at cardiac arrhythmias either showed no relationship with OSA or were retrospective case series (Level 4 evidence). The 3 studies that showed a relationship between OSA and ischemic heart disease were also low quality (Level 4 evidence) because they failed to control for important confounders. Similar problems exist for studies examining the

associations between OSA and both pulmonary hypertension and stroke. Most of those studies were cross sectional and did not control for potentially confounding variables.

Since 1997 there have been no studies published rated as Level 2 evidence or higher. Thus, at the present time, based on the available research evidence, it would be difficult to conclude that OSA is causally linked to excess mortality or to major cardiovascular or cerebrovascular morbidity.

Systemic Hypertension. It has been documented that OSA patients have elevated blood pressure during sleep, especially at the times of arousal from sleep that terminate apneic events. This is thought to be secondary to increased sympathetic nerve activity. Animal models have shown that intermittent hypoxia or intermittent airway occlusion not only causes hypertension during sleep but also sustained hypertension during the day.[7] However, in human epidemiology studies the relationship between OSA and hypertension is difficult to study because of multiple confounding variables such as obesity and alcohol consumption that are difficult to control because of their high prevalence. The studies that were reviewed by Wright et al[6] were cross sectional (Level 4 evidence) and reported conflicting results. Many of the studies did not control for smoking, alcohol, or use of antihypertensive medications.

In a very large, community-based, cross-sectional study the presence of OSA (AHI $\geq$ 30) had an odds ratio for hypertension of 1.37 ($p = 0.005$) after controlling for body-mass index, neck circumference, alcohol intake, smoking, and sex.[8] In the only prospective study to date (Level 1 evidence), a dose-response relationship was found between the severity of OSA at baseline and the odds of developing hypertension 4 years later.[9] The odds ratios were controlled for known confounding factors such as baseline hypertension status, body-mass index, neck and waist circumference, age, sex, alcohol use, and cigarette consumption. The odds ratios ranged from 1.42 for AHIs of 0.1–4.9, up to 2.89 for AHIs $\geq$ 15.0. That was the first cohort study that strongly suggested causality between sleep apnea and hypertension.

Motor Vehicle Accidents. Wright et al[6] reviewed 6 cross-sectional studies reporting an association between OSA and motor vehicle accident rates. The studies failed to control for potentially confounding variables, and some of them relied on self-reports of accidents. In the Wisconsin Sleep Cohort Study, the association between OSA and motor vehicle accident rates (using state driving statistics) was significant only among men. A dose-response relationship could not be shown, but the odds ratio for a motor vehicle accident was 3.0 for AHI $\geq$ 5.[10] Thus, at the present time the evidence is weak that OSA is a risk factor for motor vehicle accidents. Although there are numerous studies showing a relationship between OSA and reduced driving simulator performance, the relevance of those findings to estimating the risk of an OSA patient having a motor vehicle accident is unknown.

Quality of Life. The most widely used method of evaluating quality of life is a shortened version of the Medical Outcomes Study Short Form 36 (SF-36), which has 36 questions[11] and is divided into 8 domains covering a broad range of quality of life issues. It was designed to be applicable to, and therefore allow comparison between, a wide range of people with different conditions. The SF-36 evaluates both mental and physical states and measures them in several ways, including behavioral and physical functioning, social and role disability, and perceived well being.[11] There are 8 dimensions in the SF-36, each with a unique scale and weighting system:

1. Physical functioning
2. Role limitations due to physical health
3. Bodily pain
4. Social functioning
5. General mental health
6. Role limitations due to emotional problems
7. Vitality
8. General health perceptions

The Wisconsin Sleep Cohort Study (a large-scale epidemiology investigation of working adults) found that OSA patients had lower scores on several of the SF-36 domains after statistical adjustment for age, gender, body-mass index, and cardiovascular conditions.[12] Six of the domains (mental health, vitality, physical functioning, role limitations due to physical health, social functioning, and general health perceptions) showed a progressive decrement in scores in subjects with AHI $\geq$ 5, compared to those with AHI $<$ 5. The mean decrements for an AHI of 5 ranged from 2.7 $\pm$ 1.2 to 4.9 $\pm$ 1.2; for an AHI of 15 the range was from 4.2 $\pm$ 1.9 to 7.5 $\pm$ 3.6; and for an AHI of 30 the range was from 5.2 $\pm$ 2.4 to 9.3 $\pm$ 4.5. These decrements are similar to those seen for other chronic conditions such as diabetes, arthritis, angina, and hypertension.

A study of 95 OSA patients referred to a sleep center found lower scores in most SF-36 domains (but in particular in role-physical, vitality, and role-emotional) in that study group than the mean scores of a general population.[13] They were also found to improve with CPAP, almost back to the general population mean values. The profile of the SF-36 domains in OSA patients is slightly different than that of patients with other serious underlying medical conditions, but the percentage decline is of the same order of magnitude. In uncontrolled intervention studies there is always a possibility that some of the improvement is a placebo response. In a randomized, placebo-controlled crossover study of 34 patients with mild OSA

(AHI 5–15). Engleman et al observed mean improvements in SF-36 domain scores of 7–25 in patients on CPAP, compared to baseline, versus 0–17 in patients on placebo, compared to baseline.[14] The largest differences between CPAP and placebo were seen in role-physical, bodily pain, social function, and vitality. This was an unblinded study because the placebo was an oral tablet; therefore the possibility of bias still exists. In a more recent study, in which therapeutic CPAP was compared to placebo (subtherapeutic) CPAP, the vitality domain and the general health domain showed statistically significant differences between the groups.[15] To date there are no SF-36 data reported on an inception cohort. Thus, there are no Level 1 studies, but there are two Level 2b studies that provide strong evidence that OSA affects quality of life.

How Should Obstructive Sleep Apnea Be Diagnosed?

Issue of Resources

Despite the high prevalence of OSA in the general population, the majority of individuals with OSA go unrecognized by the medical community. Data from the Wisconsin Sleep Cohort study indicate that 93% of women and 82% of men with moderate to severe OSA have not been diagnosed.[16] Several factors contribute to this problem. Many physicians are not trained to conduct[17] and thus do not routinely include a sleep assessment.[18] The classic description of an OSA patient is the obese middle-aged male who is sleepy and snores, but that can be misleading because not all OSA patients are overweight, and sleepiness and snoring occur frequently in the general population. Furthermore, OSA is more common among women than previously suspected,[19] and the disorder is increasingly being recognized in the elderly[20] and in children.[21]

Compounding the issues of high prevalence and underrecognition is the high cost associated with diagnosing and treating OSA patients. This in turn needs to be weighed against the possible excess use of health care resources by undiagnosed OSA patients. A recent study found that OSA patients consume approximately twice as many health care dollars as do age- and gender-matched controls.[22] Unfortunately, that retrospective cohort study did not control for any potentially confounding variables such as obesity, comorbid illness (eg, hypertension or ischemic heart disease), or cigarette or alcohol consumption. Therefore, confirmatory evidence from a prospective cohort study is still required before a definite conclusion can be drawn about sleep apnea patients' use of health resources.

Currently, the accepted standard diagnostic test for OSA is overnight polysomnography (PSG). PSG is expensive and labor intensive and by current standards requires patients to sleep overnight in an unfamiliar sleep laboratory. Health care budgets in many jurisdictions have not accommodated the need for widespread use of PSG, so waiting lists for diagnostic evaluation in sleep laboratories are often very long. This raises the obvious question of who should undergo PSG testing. The American Sleep Disorders Association Standards of Practice Committee recommends the use of PSG in the following situations:

1. Diagnosis of patients suspected of having sleep-related breathing disorders
2. CPAP titration
3. Preoperatively, in OSA patients scheduled to undergo laser-assisted uvulopalatopharyngoplasty
4. Follow-up of patients treated with intraoral appliances or following surgery
5. For reevaluation of CPAP-treated patients after substantial weight loss or gain or if symptoms recur despite good initial response to CPAP[23]

Polysomnography and Recommendations from the American Academy of Sleep Medicine Task Force

Although a full polysomnogram that records apneas and hypopneas during sleep is considered by most to be the reference standard for diagnosing OSA, there is a large degree of variability in event definition between clinical and research labs.[24] This has led to many investigators questioning how "gold" the standard really is. Recommendations for how to score apneas and hypopneas and in particular what technology to use to record breathing disturbances during sleep have recently been published.[1] It is hoped that if investigators use similar definitions there will be a better opportunity for comparing results between studies. One of the major recommendations was to use nasal pressure as an estimate of air flow or the sum of respiratory impedance plethysmography as an estimate of tidal volume to define breathing events, rather than a thermistor. Thermistors are widely used in sleep labs, but there is a nonlinear relationship between the flow signal generated from a thermistor (which is based on changes in air temperature) and true flow measured by a pneumotachograph. Thus, current recommendations are to use a pneumotachograph, nasal pressure, or respiratory impedance plethysmography to define events (if there is a $> 50\%$ decline from baseline for > 10 s).[1] In the situation in which there is a discernible decrease in one of these signals but it does not meet the $> 50\%$ criterion, then it is recommended that an event be scored if it is associated with a decrease in oxygen saturation of $\geq 3\%$ or an arousal from sleep lasting ≥ 3 seconds.[1] These criteria closely match those used in the Wisconsin Sleep Cohort Study, in which there is published data linking AHI to adverse health outcomes.[3,9,10,12] However, it is still not possible to state with certainty the minimum AHI above which patients should be considered to have OSA. Commonly used cutoffs in the published literature are AHI ≥ 5, 10, and 15.

Alternative Modes of Diagnosis

Because of the expense of and technical expertise needed to conduct PSG, a number of alternative diagnostic modalities have been proposed. Broadly, these include partial channel PSG, ambulatory monitory devices (including oximetry), questionnaires, and clinical prediction rules.[25] In 1992 Douglas et al found that the clinical decisions they made based only on the respiratory channels from a polysomnogram (ie, without the electroencephalograph, electrooculogram, and electromyograms) were not different than the decisions made with review of the full polysomnogram.[26] Many studies have subsequently been published that have tried to evaluate different types of monitoring devices that have been proposed to replace full PSG for diagnosing OSA.

As for studies on prognosis, there are important questions that help to evaluate the evidence from diagnostic studies.[27,28] These have been separated into primary and secondary guides (Table 2).

In clinical medicine, diagnostic tests are performed to determine if a target disorder is present or absent. Often there is a reference or accepted standard test that ideally would be performed on all patients suspected of having the disorder in question. Theoretically, this would perfectly separate patients into those who have the disease and those who do not. However, a reference standard test may not be available, may be too costly, or may pose risk to the patient. In these circumstances, surrogate diagnostic tests are required as substitutes for the reference standard.

A "test result" can be the answer to a question about medical history, a physical exam observation, or the result of a laboratory test. For example, we could ask, What is the sensitivity and specificity of the symptom of snoring for the diagnosis of sleep apnea?

The operating characteristics of tests are often summarized as sensitivity (the proportion of patients with disease who have a positive test result: the "true positive" rate) and specificity (the proportion of patients without disease who have a negative result: the "true negative" rate). Using sensitivity and specificity to describe the utility of a diagnostic test has limitations, since they indicate the probability that the test result will be positive *if the patient has the disease* and the probability that the test will be negative *if the patient does not have the disease*. Clinicians cannot apply these numbers directly, because they do not know whether the patient has the disease. What the clinician needs to know is the probability that the patient actually has the disease *if* the test is positive, referred to as the positive predictive value or post-test probability of disease. The sensitivity and specificity are given by analyzing the vertical columns of a matrix, such as in Figure 1, whereas the positive and negative predictive values are obtained by analyzing the horizontal rows. Sensitivity, specificity, prevalence (or pre-test probability), and predictive values provide valuable information about a diagnostic test; however, it can be a challenge to interpret several different numbers that describe the operating characteristics of a test. A superior approach is to calculate a single number (the likelihood ratio) that directly relates how good a test is for increasing or decreasing the probability of disease. For a given level of diagnostic test result, a like-

Table 2. Guides and Grading System for Evidence About Diagnosis of Sleep Apnea

Primary Guides*

1. Was there an independent, blind comparison with a reference standard?
2. Did the patient sample include an appropriate spectrum of patients to whom the diagnostic test will be applied in clinical practice?

Secondary Guides*

1. Did the results of the test being evaluated influence the decision to perform the reference standard?
2. Were the methods for performing the test described in sufficient detail to permit replication?

Evidence Grading System† (quality of evidence in studies reporting data on prognosis)

Level 1a. A systematic review of Level 1 diagnostic studies (all of which showed consistently similar results)

Level 1b. An individual study that had:
- i) an independent blind comparison with a reference standard test
- ii) an appropriate spectrum of consecutive patients
- iii) all patients have undergone both the diagnostic test and the reference standard
- iv) the diagnostic test had high sensitivity and high specificity *or* a very high likelihood ratio for one level of a diagnostic test result and a very low likelihood ratio for another level‡

Level 2a. A systematic review of Level ≥ 2 diagnostic studies (all of which showed consistently similar results)

Level 2b. An individual study that had:
- i) an independent blind comparison with a reference standard test
- ii) *but* had a narrow spectrum of patients *or* used nonconsecutive patients
- iii) all patients underwent both the diagnostic test and the reference standard

Level 3. An independent blind comparison of an appropriate spectrum, but the reference standard was not applied to all study patients

Level 4. The reference standard was not applied independently or applied blind

Level 5. Expert opinion without explicit critical appraisal, or based on physiology, bench research, or first principles

*Adapted from References 27 and 28

†Adapted from Reference 5.

‡The sensitivity has to be high enough that a negative result (or the likelihood ratio small enough for a level of the diagnostic test result) confidently rules out the disorder *and* the specificity is high enough that a positive result (or the likelihood ratio large enough for a level of the diagnostic test result) confidently rules in the diagnosis.

A	RS + ve	RS -ve	
DT +ve	180	100	280
DT -ve	20	700	720
	200	800	1000

B	RS + ve	RS -ve	
DT +ve	360	72	432
DT -ve	40	528	568
	400	600	1000

Fig. 1. Hypothetical example comparing a reference standard test (RS) to a surrogate diagnostic test (DT). In this example the prevalence is 200/1,000 or 20% in panel A and 40% in panel B. The sensitivity is 90% and the specificity is 88% in both A and B; yet the positive and negative predicitive values in A are 64% and 97% respectively but in B they are 83% and 93%. +ve = positive. –ve = negative. (From Flemons WW, Whitelaw WA. Clinical features of obstructive sleep apnea. In: McNicholas WT, Phillipson EA, eds. Breathing disorders in sleep. London: WB Saunders; 2002, with permission.)

lihood ratio reflects the proportion of patients with the disease compared to those without. It is possible to calculate likelihood ratios for multiple levels of a diagnostic test result. This is an advantage over the approach of sensitivity and specificity, which requires separating a diagnostic result into only positive or negative results. If a patient undergoes a test and gets a result associated with a likelihood ratio of 1, this indicates the patient is no more likely to have the disease in question than he or she was prior to having the test. If the patient's test result was associated with a likelihood ratio of 0.5, he or she is one half as likely to have the disease. Generally, likelihood ratios of < 0.2 and > 10 have a very large impact on changing the probability of disease. (Table 3 summarizes the information about clinical features for diagnosing sleep apnea using likelihood ratios.)

A test with a high sensitivity (or very low likelihood ratio) is required to rule out a diagnosis, whereas a test with a high specificity (or a very high likelihood ratio) is required to rule in a diagnosis; an ideal test does both. Sensitivity/specificity and likelihood ratios modify the pre-test probability of disease to a new value (post-test probability). The pre-test probability is essentially the prevalence of the disease in the patient population under consideration. To attach a meaning to a positive test result, it is clearly necessary to know the prevalence or pre-test probability. This can be measured simply by applying the reference diagnostic test to a population of patients to determine the percentage of patients with the disease. As long as future patients are drawn from the same population, this pre-test probability is valid.

A second method of determining pre-test probability is simply to take an estimate made by experienced clinicians. For this one must assume that the clinicians in question have a broad enough experience base to enable them to give an accurate estimate of the likelihood that the patients in question have the disease.

Young et al found the prevalence of AHI $\geq$ 15 in the general adult population (age 30–60 years) to be 4.0% in females and 9.1% in males.[3] These would be appropriate numbers to use in a primary care setting. In populations of patients currently being referred to sleep centers because of sleep-related complaints, the prevalence of sleep apnea is much higher: between 40 and 60%.

Using sensitivity and specificity for clinical decision making requires that a test result be categorized simply as either positive or negative. Many disorders, including OSA, are not "yes or no" conditions. Instead, there is a continuous gradation in the test result (such as respiratory disturbance index) from zero to a large number, wherein the higher the value the more likely it is that a patient suffers from the disorder or has important health impairment. A lot of information is lost by calling a test result simply "positive" or "negative." This limitation can be partly avoided by classifying test results into multiple categories such as "negative," "mild," "moderate," or "severe." In this case, post-test probabilities for each category are calculated using likelihood ratios. As an example, a likelihood ratio of 2.0 indicates that a patient with a positive diagnostic test is twice as likely to have the disease. Ratios less than one change the pre-test probability to a lower value, whereas ratios greater than 1 change the pre-test probability to a higher value.

Mathematically, when using likelihood ratios to convert pre-test to post-test probabilities, the pre-test probability estimate must be converted to an odds expression (pre-test odds = pre-test probability/1 – pre-test probability) multiplied by the likelihood ratio to obtain the post-test odds that can then be converted back to a probability statement (post-test probability = post-test odds/post-test odds + 1). This process can be greatly simplified with the use of a nomogram.[29] Figure 2 demonstrates how likelihood ratios are calculated. Consider the same hypothetical test as in Figure 1b, but now rather than the diagnostic test being categorized as positive or negative, multiple levels of the test result are reported.

Clinical Prediction Rules. OSA patients present with a broad range of symptoms and physical findings, none of which are pathognomonic for OSA. Sleepiness, the hall-

Table 3. Diagnosis of Sleep Apnea—Likelihood Ratios for Symptoms and Physical Characteristics

Symptom/Physical Characteristic	Level	Likelihood Ratio
Nocturnal		
Snoring frequency[32]	< 3 nights per week	0.4
	≥ 3 nights per week	1.4
Loud, disruptive snoring frequency[32]	< 3 nights per week	0.5
	≥ 3 nights per week	1.7
Snoring intensity[33]	Extremely loud	3.6
	Louder than talking	1.3
	As loud as talking	0.5
	Slightly louder than heavy breathing	0.3
Partner's report of choking/gasping[32]	< 1 night per month	0.5
	1–8 nights per month	1.1
	≥ 3 nights per week	1.9
Partner's report of apneas	Yes[34,35]	1.4, 1.5
	No[34,35]	0.2, 0.5
Nocturia[35]	Yes	1.5
	No	0.6
Daytime		
Excessive daytime sleepiness[31]	Yes, against one's will	1.4
	Yes, but willingly	1.2
	None	0.8
Weight gain over previous 2 years[32]	< 10 pounds	0.8
	≥ 10 pounds	1.4
Impotence[36]	Yes	3.2
	No	0.9
Physical Examination		
Pharyngeal exam[31]	Abnormal	1.4
	Normal	0.8
Hypertension	Yes[35,34,32]	1.6, 2.2, 2.4
	No[34,35,32]	0.4, 0.6, 0.8
Body Mass Index	< 25 kg/m^2[32]	0.3
	25–30 kg/m^2[32]	0.7
	> 30 kg/m^2[34,32]	2.0, 2.3
Waist circumference[32]	< 90 cm	0.3
	90–110 cm	1.1
	> 110 cm	3.2
Waist-Hip Ratio[32]	< 0.8	0.2
	0.8–1.0	1.0
	> 1.0	2.8
Neck Circumference[32]	< 38 cm	0.5
	38–44 cm	1.1
	> 44 cm	4.1
Clinical Prediction Rule		
Sleep Apnea Clinical Score (SACS)[32]	< 5.0	0.3
	5–10.0	1.1
	10.1–15.0	2.2
	> 15.0	5.2

(From Flemons WW, Whitelaw WA. Clinical features of obstructive sleep apnea. In McNicholas WT, Phillipson EA, eds. Breathing disorders in sleep. London: WB Saunders, 2002, with permission.)

mark of OSA, has been shown in some studies to affect as many as 30–50% of community residents who do not have OSA.[30] Similarly, snoring, a symptom commonly observed in OSA patients, occurs in many people who do not have OSA, and therefore snoring is nonspecific. Obesity, increased neck circumference, and craniofacial/neck abnormalities such as retrognathia, micrognathia, tonsillar hypertrophy, and macroglossia are known to occur in OSA patients, but information is lacking about how to use specific measurements for clinical decision-making. A study by Viner et al[31] showed that expert clinical impression had low sensitivity and specificity for diagnosing OSA (52% and 70%, respectively). Many individual clinical features of sleep apnea patients have likelihood ratios close to 1 and thus have very low diagnostic utility (Table 3).

Recently, attempts have been made to identify combinations of features that together optimize the probability of detecting OSA. These combinations of diagnostic features are termed clinical prediction rules. They are developed by first identifying the individual clinical features associated with a diagnostic test result and then combining the most important features, using multivariate statistical models, into a group capable of independently predicting the diagnostic outcome of interest. Striking similarity is evident when comparing studies of sleep apnea clinical prediction rules. All investigators have included an anthropomorphic measurement in addition to bed partner reports of nocturnal breathing disturbances, such as snoring, apneas, or choking/gasping.[37] Age, gender, and hypertension have also been incorporated into some rules, to various extents. Clinical prediction rules have sensitivities as high as 95%, but their specificities tend to be low (41–63%).[37] Therefore, they can be used to help rule out important disease but cannot be used to definitively confirm a diagnosis of OSA. Predictors of sleep apnea in one clinical prediction rule include neck circumference, hypertension, habitual snoring, and bed partner reports of nocturnal gasping/choking respirations.[32] A sleep apnea clinical score of < 5 had a likelihood ratio of 0.25, with a corresponding post-test probability of 17%, whereas a score of > 15 had a likelihood ratio of 5.17, with a post-test probability of 81% (see Table 3).[32]

Unattended Ambulatory Monitoring. A number of portable monitors have been developed to assess patients for possible OSA.[25,38] These devices record single channels such as oximetry or 2 or more channels that include measurement of respiratory variables such as estimates of nasal air flow and chest/abdominal wall movement. Their potential advantages include increased availability, ease of use, reduced cost, and ability to be used in the home environment rather than in an unfamiliar sleep laboratory. However, most of the devices have not been rigorously evaluated, and most studies attempting to validate them

		RS +ve		RS -ve		Likelihood Ratio
		# of Pts	Proportion	# of Pts	Proportion	
DT Result	< 5	13	13/400 = .033	339	339/600 = .565	.033/.565 = 0.06
	5 – 10	27	27/400 = .068	189	189/600 = .315	.068/.315 = 0.2
	11 – 20	53	53/400 = .133	33	33/600 = .055	.133/.055 = 2.5
	21 – 40	129	129/400 = .323	31	31/600 = 052	.323/.052 = 6 8
	> 40	178	178/400 = .445	8	8/600 = .013	.445/.013 = 34 2
		400		600		

Fig. 2. The calculation of likelihood ratios. RS = reference standard. DT = diagnostic test. +ve = positive. –ve = negative. Pts = patients. (From Flemons WW, Whitelaw WA. Clinical features of obstructive sleep apnea. In: McNicholas WT, Phillipson EA, eds. Breathing disorders in sleep. London: WB Saunders; 2002, with permission.)

have suffered substantial weaknesses.[25] This is partly because very few studies have succeeded in achieving a consecutive and broad spectrum of subjects and some did not include a blinded assessment of the test results.[25] There has also been considerable variability in how the reference standard PSG was administered, making between-study comparisons difficult. Most of the tested diagnostic equipment has been tested in laboratory settings with simultaneous PSG monitoring rather than in the home setting—the venue in which this equipment is intended to be used. Finally, many studies have used correlation analysis to measure agreement between the diagnostic test in question and the reference standard. Correlation coefficients are not recommended for this purpose.[39] Instead, the methods proposed by Bland and Altman and Cohen are preferred.[1] An in-depth systematic review of the literature related to these devices was recently published,[25] and one of the major findings was that most studies had weak study designs that prevented a meaningful meta-analysis of their results. Thus, almost all of the published literature to date (with a few notable exceptions) on unattended, ambulatory diagnostic devices for sleep apnea would be Level 2 evidence or lower.

The most promising ambulatory monitors use oximetry and/or nasal pressure to identify breathing events during sleep. Although nasal pressure has yet to be properly validated through event-by-event comparison with an accepted standard, it remains a promising surrogate signal of air flow. It has excellent dynamic response[40] compared to thermistors, and recent evidence suggests that nasal pressure is capable of detecting air flow limitation,[41,42] which is a marker of upper airway narrowing. Furthermore, nasal prongs used to measure nasal pressure are well tolerated and easy to use, compared to signals such as respiratory inductance plethysmography, which can be cumbersome to use in obese patients because of frequent loss of signal amplitude from band displacement.

Oximetry. Series et al[43] compared nocturnal home oximetry followed by conventional in-laboratory PSG in 240 consecutive outpatients referred to their sleep clinic. Using PSG, they diagnosed OSA (defined as AHI > 10) in 110 patients. Their home oximetry device had very high sensitivity (98%), but its specificity was only 48%. This Level 1 study provides strong evidence that oximetry is useful for ruling out sleep apnea. Specificity was a problem in this study, possibly because of the type of analysis used for the oximetry signal (human recognition of brief dips in the oxygen saturation signal). A more recent Level 1 study looked at 246 patients and used an automated analysis of digitally recorded oxygen saturation sampled at 1 Hz.[44] When OSA was defined using an AHI and respiratory disturbance index of > 15, the automated analysis algorithm of the oximeter signal had a sensitivity and specificity of 98% and 88%, respectively. No study using a monitor based on oxygen saturation alone has ever reported this level of diagnostic performance. Comparisons between the oximeter and PSG were blinded and the study used recommended statistical measures. These results have to be considered preliminary, since only data included on simultaneous recordings of oximetry and PSG were reported. Although data were also collected on the use of this monitor at home, the results have not yet been published.

Nasal Pressure. A number of investigators have studied the AutoSet portable monitor (ResMed, Poway, California), which incorporates both nasal pressure (measured via nasal prongs as an estimate of air flow) and oxygen saturation (measured via oximetry).[45–48] The scoring of breathing events with this device depends solely on reduction in air flow. Results for the number of breathing disturbances

are based on an automated algorithm of flow analysis. Sensitivities and specificities vary according to the respiratory disturbance index cut-off point used, but range from 85–100% and 76–93%, respectively. All of these studies are Level 2 evidence because of their small sample sizes (n = 31–67) and lack of a true consecutive patient series. Patients were selected after examination by a sleep expert, which introduces selection bias.

Putting It All Together. Devices designed for case finding should be simple, inexpensive, have high sensitivity so that people with disease are not missed (a low false negative rate) and have adequate specificity so that false positives are minimized. The disease in question should also be important and have acceptable and effective treatment options. Clinical prediction rules and portable monitors are simple to use and are relatively inexpensive. The AutoSet system and the digital oximetry device described by Vazquez et al[44] have very high sensitivity and reasonably high specificity. As will be described in the following sections, effective OSA treatments are available. Therefore, clinical prediction rules and portable monitoring devices represent possibilities for evaluating individuals for suspected OSA. They have the potential to reduce the probability of disease in some patients to a level at which a clinician could decide not to investigate a patient for OSA in the sleep laboratory. In addition, patients found to have a high probability of disease could be spared a lengthy wait for PSG, since it has been shown that CPAP devices that adjust automatically produce treatment effects comparable to conventional CPAP devices, in which pressures are manually titrated in a sleep lab. Thus, only those patients who have an intermediate probability of disease and/or have serious comorbidity (eg, neuromuscular disease or ischemic heart disease) would require PSG. This approach has the potential to reduce some of the waiting lists for patients and save a limited resource (PSG) for complicated and severely affected patients.

How Should Obstructive Sleep Apnea Be Treated?

Treatment of OSA includes weight loss, oral appliances, CPAP, and surgical interventions, which are generally reserved for those who have failed other less invasive treatments. Until recently, evidence was limited that these treatments are effective. The systematic review written by Wright et al[6] concluded that the impact of OSA on public health had been over-emphasized and that the paucity of high-quality clinical trials evaluating CPAP did not justify its widespread use.

A number of questions have been proposed for evaluating the validity of published data on therapy. They help to determine if the results of a study represent an unbiased estimate of the treatment effect or if the results have been influenced in a systematic fashion, leading to false conclusions.[49] The questions have been divided into primary and secondary guides (Table 4).

Table 4 Guides and Grading System for Evidence About Treatment of Sleep Apnea

Primary Guides*
1. Was the assignment of patients to treatment randomized?
2. Were all patients who entered the trial properly accounted for at its conclusion?
   - Was follow-up complete?
   - Were patients analyzed in the groups to which they were randomized?

Secondary Guides*
1. Were patients, their clinicians, and study personnel "blind" to treatment?
2. Were the groups similar at the start of the trial?
3. Aside from the experimental intervention, were the groups treated equally?

Evidence Grading System† (quality of evidence in studies on therapy)

Level 1a.	A systematic review of randomized controlled trials
Level 1b.	Individual randomized controlled trials
Level 1c.	The situation in which all patients died before the therapy became available, but some now survive on it; or when some patients died before the therapy became available, but none now die on it
Level 2a.	A systematic review of cohort studies
Level 2b.	Individual cohort study (including low-quality randomized controlled trials)
Level 3a.	A systematic review of case-control studies
Level 3b.	Individual case-control studies
Level 4.	Case series and poor quality cohort and case-control studies
Level 5.	Expert opinion without explicit critical appraisal

*Adapted from Reference 49.
†Adapted from Reference 5

Weight Loss

The prevalence of obesity is increasing to epidemic proportions in North America.[50] Obesity is highly correlated with OSA and is thought to affect breathing by altering upper airway structure and function through increased pharyngeal soft tissue deposition.[51] Both dietary[52] and surgical[53] weight loss have been associated with a reduction in AHI. As such, weight loss has been a standard recommendation for treating overweight OSA patients. However, losing weight and maintaining weight-loss are difficult for most patients. Furthermore, OSA can recur in patients who have lost and then maintained a more ideal body weight.[54]

Most studies examining the effects of weight loss on severity of OSA are of low quality (≤ Level 3) due to small sample size, retrospective or cross-sectional design, or lack of adequate controls. Two studies provide legitimate evidence for recommending weight loss as part of

therapy in obese OSA patients. Smith et al[55] randomly assigned 15 patients to dietary weight loss and 8 to no therapy. After 5 months the weight loss group (average weight loss = 10 kg) experienced an average decrease in apnea index, from 55 to 29, along with an increase in daytime alertness, measured by questionnaire.[55] No significant parallel change was observed in the 8 patients who did not lose weight. A more recent, large, prospective study (Level 2 evidence) of 690 randomly selected patients looked at the relationship between weight change and change in OSA severity, as indicated by AHI.[56] Patients were followed over 4 years, and the authors controlled for sex, age, cigarette and alcohol use, and baseline body habitus measures. It was shown that a 10% weight gain predicted a 32% increase in AHI, whereas a 10% weight loss predicted a 26% decrease in AHI. Furthermore, among those with mild or no OSA, a 10% weight gain predicted a 6-fold increase in the odds of developing moderate to severe OSA, defined as AHI > 15.[56]

Biological plausibility and data from a small, controlled dietary study and a large longitudinal study[56] indicate that weight reduction can significantly reduce AHI and possibly provide subjective improvements in daytime sleepiness. Weight loss should be recommended in obese patients; although it is unlikely to cure OSA, it has the potential to reduce its severity.

Mandibular Advancement

Mandibular advancers are a type of intra-oral appliance developed for treating OSA. As a group they have been shown to be effective in eliminating snoring and reducing AHI.[57] In general, patients prefer them to CPAP.[58–60] Adverse effects are minimal, but include excessive salivation, dental malocclusion, and temporomandibular joint pain and dislocation.[61] Mandibular advancers cannot be used in patients with artificial dentition.

The American Sleep Disorders Association Standards of Practice Committee recommends the use of oral appliances in the following situations: primary snoring, mild OSA, patients with moderate to severe OSA who refuse or cannot tolerate nasal CPAP, and patients with moderate to severe OSA who refuse or are not candidates for corrective surgery.[62]

There have been no randomized placebo-controlled trials of mandibular advancing devices. Three crossover studies directly compared mandibular advancers to CPAP in patients with moderate to severe (AHI 15–55) OSA.[58–60] None of the studies achieved complete patient crossover, because of subject drop-out. All 3 studies using mandibular advancers showed significant reductions in AHI (39–51%), but the treatment effect was greater with CPAP (AHI reduced by 60–83%). Using the mandibular advancers, treatment failure (defined as inability to reduce AHI to < 10) occurred in 7 patients (28%) in one study[58] and in 8 patients (40%) in another.[60] No treatment failures occurred in patients using CPAP in either study. Mandibular advancers and CPAP achieved similar improvements in excessive daytime sleepiness assessed by questionnaire.[58,60] Lastly, patient satisfaction was greater[58,60] and adverse effects less frequent[40] with mandibular advancers than with CPAP.

Continuous Positive Airway Pressure

CPAP remains the most effective method of treating OSA. It functions by providing a pneumatic splint to the upper airway during inspiration, thereby preventing the high negative inspiratory pressures that cause pharyngeal collapse during an obstructive breathing event.[63] In 1997 Wright et al[6] systematically reviewed the literature evaluating the effectiveness of CPAP for treating OSA. At that time there was only one controlled trial[64] evaluating CPAP, which was criticized for the placebo control, an oral tablet. Oral placebos do not subject patients to the same instrumental constraints as does therapeutic CPAP.[6] However, their use in crossover studies has been justified because of the possibility that a placebo CPAP that provided air but little or no airway pressure could become apparent to subjects, thus unblinding the study.

Subsequent to the review by Wright et al, placebo CPAP devices have been developed and used in a randomized, controlled trial of CPAP.[15] These devices appear and function the same as true CPAP except that they deliver pressure ≤ 1 cm H_2O, which is unlikely to splint open the airway. Placebo CPAP has been shown to have no effect on sleep efficiency, arousal frequency, or AHI.[65] Since the first Level 1 study by Engleman et al in 1994, a number of randomized controlled studies, using both oral placebo[14,66–68] and placebo CPAP,[15,69,70] have looked at the ability of CPAP to improve objective and subjective measures of sleepiness and quality of life,[14,15,66–68] simulated driving performance,[69] and blood pressure.[68,70]

Sleepiness and Quality of Life. Engleman et al[64] studied 32 patients with moderate to severe OSA (mean AHI 28, range 7–129) over 4 weeks, using both CPAP and oral placebo (randomized placebo-controlled crossover design). Compared to placebo, CPAP resulted in decreased sleepiness and napping frequency and improvements in multiple sleep latency time. Treatment with CPAP also produced improvements in the Nottingham Health Profile quality of life questionnaire. These findings have been extended to include patients with mild OSA (AHI 5–15). Compared to oral placebo, CPAP also improves subjective daytime sleepiness and 5 of the 8 SF-36 domains in patients with mild OSA (AHI 5–15). However, no significant

differences were found in objective sleepiness measured by the maintenance-of-wakefulness test.[14]

Studies using placebo CPAP as the control indicate that CPAP substantially benefits sleepiness and quality of life. Jenkinson et al[15] randomized 53 patients to placebo CPAP and 54 patients to therapeutic CPAP. They found significant improvements in subjective sleepiness (measured by a subjective rating of sleepiness) and objective sleepiness (measured by mean maintenance-of-wakefulness test) in subjects treated with therapeutic CPAP, but not in those treated with placebo CPAP. Although therapeutic CPAP resulted in significantly greater improvements in SF-36 quality of life scores than did placebo CPAP, a small yet significant placebo effect was seen.[15]

Simulated Driving Performance. As outlined above, the evidence for a causal relationship between OSA and motor vehicle accident rates is weak. Patients with OSA do worse on driving simulators than do matched controls,[71,72] but the relevance of this is unknown. Compared to both oral placebo[64] and placebo CPAP,[15] successful treatment of OSA with therapeutic CPAP has been shown to result in statistically significant improvements in simulated driving performance. In addition, following 1 month of therapeutic CPAP, patients have quicker reaction times than controls treated with placebo CPAP.[69] Although unconfirmed, it seems plausible biologically that treatment with CPAP could reduce the number of accidents among OSA patients by reducing sleepiness and improving vigilance.

Hypertension. To date there have been no randomized controlled trials of CPAP therapy that have shown a significant impact of treatment on hypertension. A number of small clinical trials, most of which have lacked an adequate control arm, have given mixed results.[70] Two randomized placebo-controlled studies have investigated the effect of CPAP treatment of OSA on blood pressure.[68,70] The first study used a randomized crossover design to study 13 patients with both CPAP and oral placebo, and found no effect from CPAP on 24-hour ambulatory blood pressure.[68] The second study randomized 39 patients to either therapeutic (n = 21) or placebo (n = 18) CPAP. Twenty-four-hour ambulatory blood pressure was measured at baseline and following 1 and 7 days of therapy. Daytime mean arterial blood pressure decreased significantly but equally in both the active treatment and sham treatment group. Nighttime mean arterial blood pressure decreased to a greater extent in patients who received active CPAP than in those treated with placebo.[54] Systemic hypertension resulting from OSA would probably take a long time to develop; therefore, in the future, clinical trials that investigate the impact of OSA treatment on blood pressure will probably have to study large numbers of patients over a much longer period of time.

Surgery

A number of surgical procedures have been developed for treating OSA and are generally reserved for patients who have failed other less invasive modalities of treatment. The goal of surgery is to correct obstructing anatomic abnormalities and to augment the size of the upper airway. In 1996 the American Sleep Disorders Association reviewed the efficacy of upper airway surgical modifications in adults with OSA and identified the following operations used to treat OSA: nasal septal reconstruction, uvulopalatopharyngoplasty, laser midline glossectomy and lingualplasty, inferior mandibular osteotomy and genioglossal advancement with hyoid myotomy and suspension, maxillomandibular advancement osteotomy, and tracheotomy.[73]

There have been no randomized controlled trials comparing any of the surgical therapies.[74] In fact, most of the surgical literature comes from small case-series (Level 4 evidence). These studies probably contain substantial bias related to their limited sample sizes and patient follow-up, lack of controls, and patient selection. In addition, studies seldom report important outcome measures such as quality of life. A recent Cochrane Review article emphasized the need for high-quality randomized trials in the field of surgery for OSA.[74]

Uvulopalatopharyngoplasty has been the most widely used surgical procedure. In this technique, the retropalatal airway is enlarged through excision of the tonsils (if present), trimming and reorientation of the anterior and posterior tonsillar pillars, and excision of the uvula and posterior portion of the soft palate. Although uvulopalatopharyngoplasty has been shown to decrease respiratory disturbance index by an average of 38%,[75] its long-term (4–8 yr) effectiveness (defined as a $\geq$ 50% reduction in AHI and a postoperative AHI of $\leq$ 10) is $<$ 50%.[76] The procedure has been associated with substantial morbidity, including postoperative pain, bleeding, nasopharyngeal stenosis, voice change, and (rarely) death.[75]

The only true randomized trial comparing surgical and nonsurgical therapy was performed by Wilhelmsson et al.[77] Patients were randomized to either uvulopalatopharyngoplasty or treatment with a dental appliance designed to advance the mandible. Thirty-seven of 49 in the dental appliance group and 43 of 46 in the uvulopalatopharyngoplasty group completed the 12-month follow-up. Seventy-eight percent of the dental appliance group were considered treatment successes (apnea index $<$ 5 or AHI $<$ 10), compared to 51% of the uvulopalatopharyngoplasty group.

Tracheostomy remains the definitive surgical treatment for OSA because the procedure bypasses the collapsible upper airway. It is associated, however, with adverse psychological and cosmetic effects, leading to substantial emotional and physical morbidity.[78] For those who cannot tolerate CPAP or other interventions and in those patients with severe OSA associated with cardiovascular complications, tracheostomy remains an important surgical option.

Summary

OSA is a prevalent condition that affects quality of life and places patients at increased risk of developing hypertension. The risk of mortality and of cardiovascular morbidity and motor vehicle accidents among patients with untreated OSA has not been well documented. The majority of OSA patients are currently not being offered diagnostic testing and treatment—a situation that needs to change by improving professional and patient education as well as increasing diagnostic resources. There is an expanding body of evidence that supports the use of clinical prediction rules and unattended monitoring as reasonable alternatives to PSG for diagnosing OSA. The use of alternative diagnostic methods in selected patients could help alleviate the long patient waiting lists for PSG at many sleep centers. Recent randomized, placebo-controlled trials indicate that CPAP benefits quality of life, driving performance, blood pressure, and sleepiness. Mandibular advancement would appear to be a reasonable alternative therapy for patients unable to tolerate CPAP. However, the strength of the clinical evidence supporting mandibular advancement is not as strong as it is for CPAP. Preliminary evidence suggests that mandibular advancement is probably not indicated for patients with severe OSA. The efficacy of surgical intervention is not supported by randomized controlled trials and should probably be viewed as an option only when other options are not feasible. There is a strong need for larger randomized controlled trials with longer patient follow-up to verify the exact range of benefits that OSA patients can expect from the various treatment modalities.

REFERENCES

1. Sleep-related breathing disorders in adults: recommendations for syndrome definition and measurement techniques in clinical research. The Report of an American Academy of Sleep Medicine Task Force. Sleep 1999;22(5):667–689.
2. Guyatt GH, Naylor CD, Juniper E, Heyland DK, Jaeschke R, Cook DJ. Users' guides to the medical literature. XII. How to use articles about health-related quality of life. Evidence-Based Medicine Working Group. JAMA 1997;277(15):1232–1237.
3. Young T, Palta M, Dempsey J, Skatrud J, Weber S, Badr S. The occurrence of sleep-disordered breathing among middle-aged adults. N Engl J Med 1993;328(17):1230–1235.
4. Laupacis A, Wells G, Richardson WS, Tugwell P. Users' guides to the medical literature. V. How to use an article about prognosis. Evidence-Based Medicine Working Group. JAMA 1994;272:234–237.
5. Sackett DL, Strauss SE, Richardson WS, Rosenberg W, Haynes RB. Evidence-based medicine: how to practice and teach EBM. 2nd ed. Edinburgh: Churchill Livingstone; 2000:173–177.
6. Wright J, Johns R, Watt I, Melville A, Sheldon T. Health effects of obstructive sleep apnoea and the effectiveness of continuous positive airways pressure: a systematic review of the research evidence. BMJ 1997;314(7084):851–860.
7. Brooks D, Horner RL, Kozar LF, Render-Teixeira CL, Phillipson EA. Obstructive sleep apnea as a cause of systemic hypertension: evidence from a canine model. J Clin Invest 1997;99(2):106–109.
8. Nieto FJ, Young TB, Lind BK, Shahar E, Samet JM, Redline S, et al. Association of sleep-disordered breathing, sleep apnea, and hypertension in a large community-based study. Sleep Heart Health Study. JAMA 2000;283(14):1829–1836.
9. Peppard PE, Young T, Palta M, Skatrud J. Prospective study of the association between sleep-disordered breathing and hypertension. N Engl J Med 2000;342(19):1378–1384.
10. Young T, Blustein J, Finn L, Palta M. Sleep-disordered breathing and motor vehicle accidents in a population-based sample of employed adults. Sleep 1997;20(8):608–613.
11. Ware JE Jr, Sherbourne CD. The MOS 36-item short-form health survey (SF-36). I. Conceptual framework and item selection. Med Care 1992;30(6):473–481.
12. Finn L, Young T, Palta M, Fryback DG. Sleep-disordered breathing and self-reported general health status in the Wisconsin sleep cohort study. Sleep 1998;21(7):701–706.
13. Jenkinson C, Stradling J, Petersen S. Comparison of 3 measures of quality of life outcome in the evaluation of continuous positive airway pressure therapy for sleep apnoea. J Sleep Res 1997;6(3):199–204.
14. Engleman HM, Kingshott RN, Wraith PK, Mackay TW, Deary IJ, Douglas NJ. Randomized placebo-controlled crossover trial of continuous positive airway pressure for mild sleep Apnea/Hypopnea syndrome. Am J Respir Crit Care Med 1999;159(2):461–467.
15. Jenkinson C, Davies RJ, Mullins R, Stradling JR. Comparison of therapeutic and subtherapeutic nasal continuous positive airway pressure for obstructive sleep apnoea: a randomised prospective parallel trial. Lancet 1999;353(9170):2100–2105.
16. Young T, Evans L, Finn L, Palta M. Estimation of the clinically diagnosed proportion of sleep apnea syndrome in middle-aged men and women. Sleep 1997;20(9):705–706.
17. Rosen RC, Rosekind M, Rosevear C, Cole WE, Dement WC. Physician education in sleep and sleep disorders: a national survey of U.S. medical schools. Sleep 1993;16(3):249–254.
18. Ball EM, Simon RD, Tall AA, Banks MB, Nino-Murcia G, Dement WC. Diagnosis and treatment of sleep apnea within the community. The Walla Walla Project. Arch Intern Med 1997;157(4):419–424.
19. Redline S, Kump K, Tishler PV, Browner I, Ferrette V. Gender differences in sleep disordered breathing in a community-based sample. Am J Respir Crit Care Med 1994;149(3 Pt 1):722–726.
20. Ancoli-Israel S, Kripke DF, Klauber MR, Mason WJ, Fell R, Kaplan O. Sleep-disordered breathing in community-dwelling elderly. Sleep 1991;14(6):486–95.
21. Redline S, Strohl KP. Recognition and consequences of obstructive sleep apnea hypopnea syndrome. Clin Chest Med 1998;19(1):1–19.
22. Ronald J, Delaive K, Roos L, Manfreda J, Bahammam A, Kryger MH. Health care utilization in the 10 years prior to diagnosis in obstructive sleep apnea syndrome patients. Sleep 1999;22(2):225–229.
23. Practice parameters for the indications for polysomnography and related procedures. Polysomnography Task Force, American Sleep Disorders Association Standards of Practice Committee. Sleep 1997; 20(6):406–422.

24. Moser NJ, Phillips BA, Berry DT, Harbison L. What is hypopnea, anyway? Chest 1994;105(2):426–428.
25. Ross SD, Sheinhait IA, Harrison KJ, Kvasz M, Connelly JE, Shea SA, Allen IE. Systematic review and meta-analysis of the literature regarding the diagnosis of sleep apnea. Sleep 2000;23(4):519–532.
26. Douglas NJ, Thomas S, Jan MA. Clinical value of polysomnography. Lancet 1992;339(8789):347–350.
27. Jaeschke R, Guyatt G, Sackett DL. Users' guide to the medical literature. III. How to use an article about a diagnostic test. A. Are the results of the study valid? Evidence-Based Medicine Working Group. JAMA 1994;271(5):389–391.
28. Jaeschke R, Guyatt G, Sackett DL. Users' guide to the medical literature. III. How to use an article about a diagnostic test. B. What are the results and will they help me care for my patients? Evidence-Based Medicine Working Group. JAMA 1994;271(9):703–707.
29. Sackett DL, Strauss SE, Richardson WS, Rosenberg W, Haynes RB. Evidence-based medicine. How to practice and teach EBM, 2nd ed. Edinburgh: Churchill Livingstone; 2000:79.
30. Strohl KP, Redline S. Recognition of obstructive sleep apnea. Am J Respir Crit Care Med 1996;154(2 Pt 1):279–289.
31. Viner S, Szalai JP, Hoffstein V. Are history and physical examination a good screening test for sleep apnea? Ann Intern Med 1991; 115(5):356–359.
32. Flemons WW, Whitelaw WA, Brant R, Remmers JE. Likelihood ratios for a sleep apnea clinical prediction rule. Am J Respir Crit Care Med 1994;150(5 Pt 1):1279–1285.
33. Kump K, Whalen C, Tishler PV, Browner I, Ferrette V, Strohl KP, et al. Assessment of the validity and utility of a sleep-symptom questionniare. Am J Respir Crit Care Med 1994;150(3):735–741.
34. Crocker BD, Olson LG, Saunders NA, Hensley MJ, McKeon JL, Allen KM, Gyulay SG. Estimation of the probability of disturbed breathing during sleep before a sleep study. Am Rev Respir Dis 1990;142(1):14–18.
35. Rauscher H, Popp W, Zwick H. Model for investigating snorers with suspected sleep apnea. Thorax 1993;48(3):275–279.
36. Hoffstein V, Szalai JP. Predictive value of clinical features in diagnosing obstructive sleep apnea. Sleep 1993;16(2):118–122.
37. Flemons WW, McNicholas WT, editors. Clinical prediction of the sleep apnea syndrome. Sleep Med Rev: 1997;1:19–32.
38. Ferber R, Millman R, Coppola M, Fleetham J, Murray CF, Iber C, et al. Portable recording in the assessment of obstructive sleep apnea. ASDA standards of practice. Sleep 1994;17(4):378–392.
39. Altman DG. Practical statistics for medical research. London: Chapman & Hall; 1991.
40. Montserrat JM, Farre R, Ballester E, Felez MA, Pasto M, Navajas D. Evaluation of nasal prongs for estimating nasal flow. Am J Respir Crit Care Med 1997;155(1):211–215.
41. Clark SA, Wilson CR, Satoh M, Pegelow D, Dempsey JA. Assessment of inspiratory flow limitation invasively and noninvasively during sleep. Am J Respir Crit Care Med 1998;158(3):713–722.
42. Hosselet JJ, Norman RG, Ayappa I, Rapoport DM. Detection of flow limitation with a nasal cannula/pressure transducer system. Am J Respir Crit Care Med 1998;157(5 Pt 1):1461–1467.
43. Series F, Marc I, Cormier Y, La Forge J. Utility of nocturnal home oximetry for case finding in patients with suspected sleep apnea hypopnea syndrome. Ann Intern Med 1993;119(6):449–453.
44. Vazquez JC, Tsai WH, Flemons WW, Masuda A, Brant R, Hajduk E, Whitelaw WA, Remmers JE. Automated analysis of digital oximetry in the diagnosis of obstructive sleep apnoea. Thorax 2000;55(4): 302–307.
45. Bradley PA, Mortimore IL, Douglas NJ. Comparison of polysomnography with ResCare Autoset in the diagnosis of the sleep apnoea/hypopnoea syndrome. Thorax 1995;50(11):1201–1203.
46. Fleury B, Rakotonanahary D, Hausser-Hauw C, Lebeau B, Guillemnault C. A laboratory validation study of the diagnostic mode of the Autoset system for sleep-related respiratory disorders. Sleep 1996; 19(6):502–505.
47. Kiely JL, Delahunty C, Matthews S, McNicholas WT. Comparison of a limited computerized diagnostic system (ResCare Autoset) with polysomnography in the diagnosis of obstructive sleep apnoea syndrome. Eur Respir J 1996;9(11):2360–2364.
48. Gugger M. Comparison of ResMed AutoSet (version 3.03) with polysomnography in the diagnosis of the sleep apnoea/hypopnoea syndrome. Eur Respir J 1997;10(3):587–591.
49. Guyatt GH, Sackett DL, Cook DJ. Users' guides to the medical literature. II. How to use an article about therapy or prevention. A. Are the results of the study valid? Evidence-Based Medicine Working Group. JAMA 1993;270(21):2598–2601.
50. Mokdad AH, Serdula MK, Dietz WH, Bowman BA, Marks JS, Koplan JP. The spread of the obesity epidemic in the United States, 1991–1998. JAMA 1999;282(16):1519–1522.
51. Strobel RJ, Rosen RC. Obesity and weight loss in obstructive sleep apnea: a critical review. Sleep 1996;19(2):104–115.
52. Rubinstein I, Colapinto N, Rotstein LE, Brown IG, Hoffstein V. Improvement in upper airway function after weight loss in patients with obstructive sleep apnea. Am Rev Respir Dis 1988;138(5):1192–1195.
53. Peiser J, Lavie P, Ovnat A, Charuzi I. Sleep apnea syndrome in the morbidly obese as an indication for weight reduction surgery. Ann Surg 1984;199(1):112–115.
54. Pillar G, Peled R, Lavie P. Recurrence of sleep apnea without concomitant weight increase 7.5 years after weight reduction surgery. Chest 1994;106(6):1702–1704.
55. Smith PL, Gold AR, Meyers DA, Haponik EF, Bleecker ER. Weight loss in mildly to moderately obese patients with obstructive sleep apnea. Ann Intern Med 1985;103(6 Pt 1):850–855.
56. Peppard PE, Young T, Palta M, Dempsey J, Skatrud J. Longitudinal study of moderate weight change and sleep-disordered breathing. JAMA 2000;284(23):3015–3021.
57. Schmidt-Nowara W, Lowe A, Wiegand L, Cartwright R, Perez-Guerra F, Menn S. Oral appliances for the treatment of snoring and obstructive sleep apnea: a review. Sleep 1995;18(6):501–510.
58. Ferguson KA, Ono T, Lowe AA, Keenan SP, Fleetham JA. A randomized crossover study of an oral appliance vs nasal-continuous positive airway pressure in the treatment of mild-moderate obstructive sleep apnea. Chest 1996;109(5):1269–1275.
59. Clark GT, Blumenfeld I, Yoffe N, Peled E, Lavie P. A crossover study comparing the efficacy of continuous positive airway pressure with anterior mandibular positioning devices on patients with obstructive sleep apnea. Chest 1996;109(6):1477–1483.
60. Ferguson KA, Ono T, Lowe AA, al-Majed S, Love EL, Fleetham JA. A short-term controlled trial of an adjustable oral appliance for the treatment of mild to moderate obstructive sleep apnoea. Thorax 1997; 52(4):362–368
61. Henderson JH 2nd, Strollo PJ. Medical management of obstructive sleep apnea. Prog Cardiovasc Dis 1999;41(5):377–386.
62. Practice parameters for the treatment of snoring and obstructive sleep apnea with oral appliances. American Sleep Disorders Association. Sleep 1995;18(6):511–513.
63. Bahammam A, Kryger M. Decision making in obstructive sleep-disordered breathing. Putting it all together. Clin Chest Med 1998; 19(1):87–97.
64. Engleman HM, Martin SE, Deary IJ, Douglas NJ. Effect of continuous positive airway pressure treatment on daytime function in sleep apnoea/hypopnoea syndrome. Lancet 1994;343(8897):572–575.
65. Farre R, Hernandez L, Montserrat JM, Rotger M, Ballester E, Navajas D. Sham continuous positive airway pressure for placebo-controlled studies in sleep apnoea (letter). Lancet 1999;353(9159):1154

66. Engleman HM, Martin SE, Deary IJ, Douglas NJ. Effect of CPAP therapy on daytime function in patients with mild sleep apnoea/hypopnoea syndrome. Thorax 1997;52(2):114–119.
67. Engleman HM, Martin SE, Kingshott RN, Mackay TW, Deary IJ, Douglas NJ. Randomised placebo controlled trial of daytime function after continuous positive airway pressure (CPAP) therapy for the sleep apnoea/hypopnoea syndrome. Thorax 1998;53(5):341–345.
68. Engleman HM, Gough K, Martin SE, Kingshott RN, Padfield PL, Douglas NJ. Ambulatory blood pressure on and off continuous positive airway pressure therapy for the sleep apnea/hypopnea syndrome: effects in "non-dippers." Sleep 1996;19(5):378–381.
69. Hack M, Davies RJ, Mullins R, Choi SJ, Ramdassingh-Dow S, Jenkinson C, Stradling JR. Randomised prospective parallel trial of therapeutic versus subtherapeutic nasal continuous positive airway pressure on simulated steering performance in patients with obstructive sleep apnoea. Thorax 2000;55(3):224–231.
70. Dimsdale JE, Loredo JS, Profant J. Effect of continuous positive airway pressure on blood pressure: a placebo trial. Hypertension 2000;35(1 Pt 1):144–147.
71. Findley LJ, Levinson MP, Bonnie RJ. Driving performance and automobile accidents in patients with sleep apnea. Clin Chest Med 1992;13(3):427–435.
72. George CF, Boudreau AC, Smiley A. Simulated driving performance in patients with obstructive sleep apnea. Am J Respir Crit Care Med 1996;154(1):175–181.
73. Sher AE, Schechtman KB, Piccirillo JF. The efficacy of surgical modifications of the upper airway in adults with obstructive sleep apnea syndrome. Sleep 1996;19(2):156–177.
74. Bridgman SA, Dunn KM. Surgery for obstructive sleep apnoea. Cochrane Database Syst Rev 2000;(2):CD001004.
75. Sher AE. Surgical management of obstructive sleep apnea. Prog Cardiovasc Dis 1999;41(5):387–396.
76. Janson C, Gislason T, Bengtsson H, Eriksson G, Lindberg E, Lindholm CE, et al. Long-term follow-up of patients with obstructive sleep apnea treated with uvulopalatopharyngoplasty. Arch Otolaryngol Head Neck Surg 1997;123(3):257–262.
77. Wilhelmsson B, Tegelberg A, Walker-Engstrom ML, Ringqvist M, Andersson L, Krekmanov L, Ringqvist I. A prospective randomized study of a dental appliance compared with uvulopalatopharyngoplasty in the treatment of obstructive sleep apnoea. Acta Otolaryngol 1999;119(9):503–509.
78. Powell NB, Riley RW, Robinson A. Surgical management of obstructive sleep apnea syndrome. Clin Chest Med 1998;19(1):77–86.

Discussion

MacIntyre: To increase patient compliance with mask positive pressure, you might try BiPAP [bi-level positive airway pressure], which is inspiratory pressure along with the baseline expiratory pressure—sort of a pressure support or pressure assist mode. Is there much data supporting that contention?

Flemons: I didn't go looking for that specifically, but my feeling about that is like a lot of things: everybody says it, but nobody actually does the study to prove it. I would think it would apply to only a small percentage of patients, so I think that kind of study would be difficult to do.

MacIntyre: In practical terms, in the United States, you can get a BiPAP machine paid for by Medicare if you "fail CPAP."

Flemons: Technically speaking, we can ask our government to do the same thing now, though I'm not sure we actually have the evidence to back that up.

Guyatt: In terms of improving compliance, I noticed in your data that you had about 70–80% of the people complying, but by your estimate of your own minimally important difference, only half of the people actually benefited. So if half of the people don't actually get an important benefit, are we really doing a good thing by improving compliance? It would be conceivable to me that the people who don't comply are the half that aren't benefiting and that the most efficient thing would be to take their machines and give them to people who will use them. So I'm wondering in the trials of compliance-enhancing strategies if compliance is really the right outcome, and maybe the right outcome should be improvement in quality of life, particularly if you're suggesting that some of the people, or even those who continue it, are not getting important benefits.

Flemons: I think that's a fair comment. We are just starting to try to get some data about that. Right now we don't even know whether improved quality of life would predict that people would use their machines more often. So I think when we collect that kind of data on larger numbers of patients we might be able to tease out some of those factors. I guess the other thing is that we don't understand human behavior very well, as you pointed out. So I'm not quite sure what it is that motivates people to use this treatment.

Guyatt: Is anybody monitoring the quality of life of the patients' spouses? That might be a possible predictor of compliance.

Flemons: It's interesting that you mention that. We spent the last year and a half trying to develop a quality of life index for patients' spouses, and the most interesting thing was when we sat down with them during the initial stages to find out what was actually important to them, we got an earful. We have just looked at the data in a preliminary fashion. We don't see tremendous improvements in the quality of life of the spouses, not like we do for patients. I'm not quite sure that spouses can actually separate what it is that is related to sleep apnea versus what it is about 30 years of living with somebody they would have maybe not preferred to live with in the first place. I sometimes feel I should have taken a course in marriage counseling before

I ever went into medicine. You know you're in trouble when you ask somebody, "So what brings you here?" and they turn around and say, "Ask her." I get that about 3 times a clinic. Initially I thought that if spouses' quality of life improved, everybody would be happier, that this would probably predict long-term compliance. That may still be the truth. When both of them get better, there may be a big incentive to continue to use CPAP. It's an interesting area that awaits further data to figure out what it is that convinces someone to use this type of treatment.

Pierson:* To be the devil's advocate, it seems to me there are some pretty strong parallels between the treatment for OSA and the use of, say, inhaled nitric oxide in ARDS. That is, you've shown us Level 1 evidence that quality of life is impaired in people with OSA, just like we know that ARDS is a bad thing and kills a lot of people. You've shown us that you can tell in 3 minutes whether CPAP is going to be effective in ablating sleep apneas in the lab, and we can show with inhaled nitric oxide in a very few minutes that the arterial partial pressure of oxygen goes up. What we need desperately, I think, is to find out in the long-run and in the big picture whether people with sleep apnea who receive CPAP turn out to be any better off in the end. It seems that, with the Level 1 data on impairment of quality of life before treatment, this is a good setting for doing outcome studies to determine whether individual patients—and society, who's paying for all of this—benefit from these fairly intrusive and expensive therapies.

Flemons: I think those are all fair comments. We've only had one trial to date that included sham CPAP control. If you ask people in sleep medicine, "Do you need sham CPAP?" they'd say absolutely not. Nobody would use this treatment if they weren't getting some benefit from it, so it's just a question of how do you measure the benefit. Clearly, when sham CPAP was used, they noticed, just like everything else, that there's a big placebo effect. So I think more trials do need to be done to define exactly what you said, David, that quality of life is the most important issue. How much is it improved? What percentage of patients does it improve? What predicts those patients?

I would take issue that this is an expensive treatment. These machines can be bought for under $1,000 (Canadian). In fact, when we buy them for our Provincial program, they cost in the range of $600. They last for over 5 years, and you actually know who *uses* it, so you can take the machine away from people who don't use it. I don't know of another treatment in medicine that costs under $100 per year (amortized over 5 years) where you can target it just to the people who use it.

I would say it's important to define the placebo effect, but when I put on my clinical hat, I'm not so concerned about that. I think that overall this will prove to be a beneficial treatment. We do need the trials to prove it, but this is a treatment where you really can target it to the people who are going to use it. We need long-term studies to determine patients' quality of life at 6 months and 1 year. My hunch is that patients will continue to show an improvement in quality of life, and that we'll be able to justify long-term treatment because of that.

Rubenfeld: I think this is an area also where the primary care physicians are receiving conflicting information and messages. We see a lot of patients referred to our clinic on an urgent basis for sleep apnea evaluation. We also have the same at our public hospital: the same delay for evaluations. I think there's a great deal of education needed. I also think the primary care providers have the sense that they're missing this epidemic. They hear the numbers like 4% of the population, 20% or 50% of obese men, and I think they're having the sense that they need to approach the patient who might have sleep apnea in the same way they do patients who have severe hyperlipidemia or severe hypertension. What kinds of educational activities are going on for the referring primary care physician?

Flemons: In 1993 Bill Dement was able to get the attention of the United States Congress and point out that there is on average about 1 hour of sleep disorders education in medical schools; so in fact there is hardly any instruction on it during medical training. And there really is no plan for continuing medical education about sleep medicine. My understanding is that Congress accepted that and started putting some things in place, but I'm not aware of a consistent plan or consistent strategy at this point to actually address the need. I think the problem is that sleep medicine has been struggling for recognition, so they've been willing to say anything and everything in order to get the recognition. Now that they've got it, they don't want it, because a lot of what they said may have been overstating the case.

For example, now we have regulations about driving, so primary care practitioners should be concerned about what that means for their patients, what it means for *them* if they miss it and one of their patients crashes a car. This is a potential area for litigation. I think we should be a lot more careful with what we conclude from very poor data in terms of creating public policy and in terms of what we tell our patients or the primary care

*David J Pierson MD FAARC, Division of Pulmonary and Critical Care Medicine, Department of Medicine, University of Washington, Seattle, Washington.

providers about what they should be acting on and why. So I think there's an education phase that needs to go on for the sleep medicine doctors first, and then we need to figure out what we tell the primary care providers and the patients.

Rowe: As a member of the Cochrane review group that was involved with the sleep apnea review,[1] I know there's no question that it created a lot of controversy. One of your comments was that people in sleep medicine said that "Wright was wrong." It sounds like it's really stimulated the sleep apnea and sleep lab profession to get their house in order. The reality is that the recommendations that came out of the review were very conservative. They essentially didn't say close all sleep labs and that all people in sleep research were misleading us! They said, "We need more evidence." So the reviews never make recommendations, or *shouldn't* make recommendations. They should provide the evidence and challenge the profession to come up with the evidence to justify what's being done. I think, in fact, you should give them an award.

REFERENCES

1. Wright J, White J, Ducharme F. Continuous positive airways pressure for obstructive sleep apnoea(Cochrane review). In: The Cochrane Library, 4, 2001. Oxford: Update Software.

Flemons: I wouldn't disagree with that at all, Brian. I think it's the best thing that's happened to this field since they first discovered that people stopped breathing at night. I think the concern about the review came mostly from physicians in Britain, because they perceived that this was going to be used as a reason not to fund what they considered a very viable treatment alternative, CPAP, for their patients. They took this very personally. It was a case where people who were *not* trained in evidence-based methods thought that they were doing all the right things, and they didn't like to be criticized. From my perspective, I think it was the right thing to publish. We can argue about interpretation of study results here and there, but I think overall their conclusions were by and large correct. I think it has actually helped people who want to do sleep research, because all you have to do to a funding agency is say "We want to do this randomized controlled trial because of what Dr Wright said." I think it was the right thing to publish, and I think it was helpful.

Rowe: Some funding agencies, particularly the MRC [Medical Research Council] in the United Kingdom, require a systematic review to form the introduction or the background for a trial. I've reviewed for them, and if you don't have a systematic review as the foundation for your trial, then it doesn't get funded. I would say, again, that that systematic review provided the appearance of equipoise. I don't know if Dr Tonelli is going to talk about equipoise, but certainly there was this observation that insufficient evidence existed. So we needed more research. I think the funding agencies at that point would agree that you have to conduct randomized controlled trials to show beneficial effects. That's where a lot of the drive for future research comes from.

Flemons: I agree. I think it was the right thing to do and created a lot of controversy. There's nothing better for a field than to create controversy and challenge people.

The Limits of Evidence-Based Medicine

Mark R Tonelli MD MA

Introduction
The Relationship Between Clinical Research and Clinical Practice
Conceptual Errors
Bridging the Gap Between Evidence and Practice
Summary

The importance of clinical research for the practice of clinical medicine is immense and undeniable. Yet the type of knowledge gained from clinical research, referred to here as "empirical evidence," is itself insufficient to provide for optimal clinical care. A gap exists between empirical evidence and clinical practice. Proponents of evidence-based medicine have clearly acknowledged one aspect of this gap: the part that requires the consideration of values, both patient and professional, prior to arriving at medical decisions. Not as clearly recognized, however, is the gap that exists due to the fact that empirical evidence is not directly applicable to individual patients, as the knowledge gained from clinical research does not directly answer the primary clinical question of what is best for the patient at hand. Proponents of evidence-based medicine have made a conceptual error by grouping knowledge derived from clinical experience and physiologic rationale under the heading of "evidence" and then have compounded the error by developing hierarchies of "evidence" that relegate these forms of medical knowledge to the lowest rungs. Empirical evidence, when it exists, is viewed as the "best" evidence on which to make a clinical decision, superseding clinical experience and physiologic rationale. But these latter forms of medical knowledge differ in kind, not degree, from empirical evidence and do not belong on a graded hierarchy. As they differ in kind, these other forms of medical knowledge can be viewed as complementary to empirical evidence and their incorporation necessary to overcome the intrinsic gap noted above. Clinicians, then, need to incorporate knowledge from 5 distinct areas into each medical decision: (1) empirical evidence, (2) experiential evidence, (3) physiologic principles, (4) patient and professional values, and (5) system features. The relative weight given to each of these areas is not predetermined, but varies from case to case. *Key words: evidence-based medicine, clinical research, clinical practice, evidence, values.* [Respir Care 2001;46(12):1435–1440]

Introduction

The development and promulgation of evidence-based medicine (EBM), which focuses on the development, acquisition, critical appraisal, and incorporation of evidence derived from clinical research into clinical practice, promises a more uniform and scientific foundation for clinical practice.[1] The popularity of EBM, at least in concept, is undeniable. Since 1992, when the term "evidence-based medicine" was introduced into the medical lexicon, a MEDLINE search now reveals over 4,900 citations. Ac-

Mark R Tonelli MD MA is affiliated with the Division of Pulmonary and Critical Care Medicine, Department of Medicine, and the Department of Medical History and Ethics, University of Washington, Seattle, Washington.

A version of this report was presented by Mark R Tonelli MD MA at the RESPIRATORY CARE Journal Conference, Evidence-Based Medicine in Respiratory Care, April 20–22, 2001, Banff, Alberta, Canada.

Correspondence: Mark R Tonelli MD MA, Division of Pulmonary and Critical Care Medicine, University of Washington, Box 356522, Seattle WA 98195-6522. E-mail: tonelli@u.washington.edu.

ceptance and praise has been particularly forthcoming from academic medicine, where the focus has been on training a new generation of clinicians in the skills required to practice EBM. The enthusiasm for EBM follows, in part, from the recognition that well-designed clinical studies have the power to generate sound medical knowledge and to positively influence medical care. As Drs Montori and Guyatt note in their introduction to EBM,[2] numerous examples can be cited of well-designed clinical trials that have resolved longstanding medical controversies or shown that particular interventions are more likely to harm than do good.

Yet despite the appeal and advantages of EBM, several authors have sounded more cautionary notes.[3–7] Although these critiques of EBM have focused on multiple facets of EBM, I will assert here that EBM remains limited primarily by one fact: The type of knowledge gained from clinical research and systematic reviews is not directly applicable to the care of individual patients. This gap between clinical research and clinical practice cannot be closed without the incorporation of alternative forms of medical knowledge, including clinical experience (both personal and that of experts), physiologic rationale, and understanding of patient and professional values. Proponents of EBM have, in fact, acknowledged the validity of some of these critiques, and the definition of EBM has shifted from "de-emphasizing" nonevidentiary forms of medical knowledge,[1] such as clinical experience and pathophysiologic rationale, to "integrating" evidence along with some types of nonevidentiary knowledge in clinical decisions.[8] Thoughtful proponents of EBM, such as Dr Guyatt, call for the "conscientious and judicious" use of evidence, but go no further in explaining what that statement means. Unfortunately, it is not self-evident. Instead, the sole focus of the EBM literature remains on the use of evidence from clinical trials and systematic reviews, telling us little or nothing about how to actually integrate alternative forms of medical knowledge into clinical practice. As a result of this limited emphasis, EBM fails to provide an adequate account of optimal medical practice.

Understanding the nature of the gap between clinical research and clinical practice allows for a discussion of the approaches that might allow the gap to be bridged. After briefly describing this gap in philosophical terms and providing clinical examples that center on subject matter contained in other articles in this issue of Respiratory Care, I will propose and briefly defend one approach to clinical decision-making that gives no priority to empirical evidence derived from clinical research.

The Relationship Between Clinical Research and Clinical Practice

The gap between clinical research and clinical practice can be understood in at least 2 ways.[9] First, the type of knowledge we gain from well-designed clinical trials and systematic reviews is not the kind of knowledge we need when we face a particular clinical problem. Clinical research methods, and particularly the randomized controlled trial, provide powerful tools for determining the efficacy of an intervention by eliminating the background noise created by individual variability in the way disease presents and healing occurs. This provides a type of empirical knowledge that tells us something about how an intervention affects an "average" patient or what would probably result from the application of an intervention across a population. The question faced by clinicians, however, is not whether a therapy works on average (although this might be an appropriate question for the Food and Drug Administration or a third-party payer), but whether it will work in the patient at hand. At best, clinical research can provide for us some probabilistic information, but it can never directly answer a specific clinical question. The type of knowledge gained from clinical research is informative but insufficient for clinical decision-making.

The importance of this knowledge gap between clinical research and clinical practice depends primarily on the importance of individual variability in the healing process. If individual variability is unimportant, then the knowledge gap is relatively unimportant. If there is wide individual variability in the presentation of disease and/or response to therapy, then the gap may render the results of a large-scale trial almost useless in clinical decision-making. For instance, Dr Dean Hess discusses the relative paucity of clinical data regarding the efficacy of airway clearance techniques, but notes the wide variability of individual responses to particular modalities.[10] This wide variability and the idiosyncratic responses to different clearance techniques seen clinically with cystic fibrosis (CF) patients, for instance, does not bode well for clinical research in that area. First, the variability complicates the performance of clinical trials, requiring large numbers to overcome the inherent "background noise." More importantly, the individual variability would severely limit the practical value of any empirical knowledge generated from a standard clinical investigation. Imagine we did have a large randomized controlled trial that showed an average improvement in FEV_1 (forced expiratory volume in the first second) and symptom scores and fewer hospitalizations in CF patients using the flutter device than in those using the positive expiratory pressure (PEP) device. One might easily misinterpret such a study as proof that flutter is better than PEP in CF and should be used preferentially for that disease. Yet such a study would demonstrate no such thing. Given the variability of response among individuals, it is almost certain that some subjects who received PEP would have done better with flutter and vice versa. If the responses are truly idiosyncratic—that is, no measurable differences among individuals predict response

to therapy, or if the study is unable to find any measurable predictors (even if they exist)—then it provides very little information to guide clinical decisions. Although the imaginary study shows flutter better on average than PEP, a large percentage of individuals with CF would do better with PEP. In deciding which form of airway clearance to use in a particular CF patient, the study provides little assistance. This limitation holds for all clinical trials, with the exception of the *n* of 1 trial. To the extent that individual differences important to the outcome are either unmeasurable or are not accounted for, a gap between clinical research and clinical practice remains.

The gap between clinical research and clinical practice is an ethical gap as well. Dr Guyatt suggests that EBM has made it clear that values are important to clinical decision making. Though I am quite pleased and relieved to see EBM explicitly acknowledging the importance of values in medicine, I would note that we did not require EBM to recognize that importance. A traditional distinction exists in moral philosophy between statements of fact and statements of value, and general consensus exists that statements of value cannot follow directly from statements of fact. That is, value judgments need to be included in any argument from facts if we hope to arrive at a conclusion regarding what ought to be done in a particular situation. In medicine, this means that knowledge derived from clinical research is never ethically prescriptive; clinical research does not tell us what we ought to do. To make the jump from research to practice we need to insert some values—those of the patient, of the profession, and/or of society. No clinical decision is exempt from the need for consideration of values. Although certain end points of clinical research, such as improved survival, might seem, at first pass, to be unequivocally good and desirable, even demonstrating that a treatment lowers mortality does not mean it should be uniformly applied. Society or payers might balk at expensive interventions that provide only marginal survival benefits, and individuals often do not wish for life-prolonging measures when their quality of life has fallen below an acceptable minimum. Low-stretch ventilation improves survival in acute respiratory distress syndrome (ARDS), but what if the associated hypoxemia leads to greater cognitive deficit in survivors? What we should do in such a situation is determined not by the evidence but by how we value an increased risk of impaired survival relative to an increased risk of death.

In the end, clinical research alone does not provide us with the type of knowledge we need to make decisions about the care of individuals, nor is it applicable without an understanding of social, professional, and personal goals, values, and preferences. The clinician requires more tools than EBM has thus far provided in order to bridge that gap.

Conceptual Errors

The EBM movement has made it clear that knowledge of empirical evidence derived from relevant clinical research is a necessary condition for the practice of sound clinical medicine. But the knowledge and value gap between such evidence and the care of individuals demonstrates that knowledge of clinical research is insufficient to guarantee the provision of optimal clinical care. Proponents of EBM appear to realize this and now speak less about "de-emphasizing" alternative forms of medical knowledge, instead telling practitioners that they need to "integrate" evidence into practice. In their description of EBM, Drs Montori and Guyatt demand that clinicians conscientiously and judiciously use evidence, though little is said about what conscientious and judicious use of evidence looks like.[2]

Proponents of EBM have also broadened their view of what constitutes evidence, including unsystematic clinical experience and physiology,[11] types of knowledge that were originally set outside the realm of evidence.[1] But in broadening the concept of evidence, EBM proponents have felt the need to clearly define a hierarchy of evidence, such as appears in Table 1, from Drs Montori and Guyatt's introduction to EBM (in the November 2001 issue of Respiratory Care).[2] These hierarchies (and there are multiple different versions promulgated) claim that some forms of evidence are of higher quality than other forms. Furthermore, these hierarchies are advanced with either an explicit or implicit claim that once a higher level of evidence is obtained, lower level evidence is superseded and becomes valueless. Two fundamental errors undermine that approach. First, hierarchies that lump and grade evidence are based on an assumption that each class of "evidence" is sufficiently similar to the others to allow for a universal judgment that, for instance, evidence from randomized controlled trials is always "better" evidence than that gained from clinical experience (see Table 1). The philosophical claim that various types of evidence can be graded in such a fashion is neither "evidence-based" nor scientific in any sense of the word; it simply represents a philosophical

Table 1. Hierarchy of Evidence: Therapy or Prevention

n of 1 randomized trials
Meta-analyses of randomized trials
Randomized controlled trials
Systematic reviews of observational studies
Observational studies
Physiologic studies
Unsystematic clinical observations

(From Reference 2)

stance that, unfortunately for the EBM movement, is untenable. The problem with the hierarchical approach to evidence is that proponents of EBM have now included in their hierarchies types of "evidence" that differ in kind from one another. That is, there is little problem with hierarchies of evidence that deal only with empirical evidence gained from various types of clinical trials and observational studies, as evidence from large controlled trials is sufficiently similar to, say, that gained from systematic observational studies to allow for direct comparison. But by trying to include clinical experience and physiologic rationale under the umbrella of "evidence," EBM makes the classic mistake of trying to compare apples and oranges. Experiential knowledge is different in kind from that derived from empirical research;[12] reasoning from physiologic theory is different in kind from reasoning from epidemiologic observations. One can call them all "evidence," but that does not allow them to be graded on a scale from best to worst.

The second error follows from the first. By assuming that all forms of medical knowledge can be seen as evidence and placed in a hierarchical fashion, EBM suggests that better evidence supersedes lesser evidence, rendering the latter superfluous. In the words of Drs Montori and Guyatt, evidence at the top of the hierarchy always has a "greater impact" on clinical decision-making than that nearer the bottom.[2] No possibility appears to exist for personal clinical experience to trump the results of a randomized controlled trial if the two appear to conflict, for the latter always represents "better" evidence and we are compelled by EBM to act in accordance with the "best available evidence."[13] Under this view, personal clinical experience or physiologic reasoning remain valuable only when there is a lack of evidence of a "better" sort. But understanding that experiential knowledge and physiologic reasoning are different in kind from empirical evidence allows for each to play a role in a particular clinical decision.

Proponents of EBM are likely to respond to the criticism outlined above by claiming that I misunderstand EBM, that it does not devalue clinical experience or other forms of medical knowledge as I claim it does. But EBM cannot simply define itself in ways that are internally inconsistent and then dismiss critique as misguided. By broadly defining "evidence," EBM becomes dependent on arbitrary and decidedly non-evidence-based assumptions of what things to cover under that umbrella. And without hierarchies of evidence, the tenets of EBM collapse. Yet the hierarchies, by the very nature of being hierarchies, devalue the "lower" forms of evidence relative to the higher. EBM simply cannot have it both ways: it cannot claim to represent a "new paradigm" founded on the primary value of empirical evidence and not devalue alternative forms of medical knowledge.

Bridging the Gap Between Evidence and Practice

As noted above, the gap between clinical research and clinical practice represents both a knowledge gap and a values gap. EBM clearly now recognizes the values gap and cautions all practitioners that patient preferences and values must be incorporated into clinical decision-making.[2] A branch of EBM now strives to find a more explicit and objective way to incorporate values into decision-making, through the use of standardized values assessment tools. The ultimate success of this "patient utilities" movement remains doubtful, but a discussion of the advantages and disadvantages of that approach is beyond the scope of this paper.[14]

Bridging the knowledge gap has garnered less attention, as the gap is not fully acknowledged by many in EBM. Part of the gap is due to the relative paucity of empirical evidence to help guide medical decisions, and this aspect is often vocalized by proponents of EBM, virtually always followed by a call for more funding to perform clinical research. The fact that the knowledge gained from clinical research is not directly applicable to individual patients is not clearly acknowledged. Yet, regardless of the quality and quantity of empirical evidence, this gap will remain and clinicians need a methodology to help them overcome it.

Overcoming this fundamental limitation of EBM depends on the recognition that current hierarchies of evidence, with claims of what universally counts as "best evidence," are fundamentally flawed. Recognizing that experiential knowledge and physiologic understanding are separate and distinct forms of medical knowing, not simply lower forms of evidence, allows for the incorporation of those types of reasons and reasoning into every clinical decision about an individual patient. That is, experiential and physiologic knowledge are not superseded by the knowledge gained from even large, well-designed clinical trials, but rather remain necessary to help overcome the intrinsic gap between clinical research and clinical practice.

Each type of medical knowledge, whether empirical, experiential, or physiologic, has its own set of strengths and limitations. No single type of knowledge, by itself, allows for the optimal practice of clinical medicine. Sound clinical judgment, then, is the quality that allows for the incorporation of various forms of medical knowledge and reasoning into a particular decision.[15] The process described here differs fundamentally from the current expositions of EBM because no priority is given to empirical evidence over other forms of medical knowledge. That is, personal clinical experience or physiologic rationale may at times be compelling enough to warrant an action in apparent contradiction to the empirical evidence, not simply in its absence. For instance, the current best evidence suggests

that low-stretch ventilation improves survival in ARDS, compelling many clinicians to use low tidal volume for all ARDS patients. Although this strategy is well-tolerated in aggregate, certain individual patients may not benefit from the intervention. What to do with the ARDS patient who, when ventilated with low-tidal volume, experiences cardiac arrhythmias as his pH falls to 7.25? The best evidence suggests that low-stretch ventilation is better for the "average" ARDS patient, but certainly does not tell us that it is better for all ARDS patients. Do we ignore the physiologic complications in our individual patient, or do we increase the tidal volume despite the empirical evidence of associated higher mortality? Are we allowed, in EBM, to trump the evidence for physiologic reasons? Based on clinical experience? Is this what is meant by a "conscientious and judicious" use of the evidence?

If we dismiss the current hierarchies of EBM and consider types of medical knowledge that differ in kind separately, 5 topics relevant to clinical decision-making can be distinguished (Table 2).

In any given clinical situation, the relative weight given to each of these particular areas will vary. No topic area is necessarily determinative. Many times, when each of the topic areas points in the same direction, decisions will be relatively simple. When the empirical evidence, personal experience, expert opinion, and physiologic understanding coincide, a recommendation is straightforward and the course of action determined only by the patient's willingness and the availability of the intervention. At other times, as in the case described above of the ARDS patient with arrhythmias, empirical evidence may conflict with personal experience or physiologic reasoning, and we are left to determine which is more compelling. This defines the essence of sound clinical judgment: how we weigh different forms of medical understanding in order to come to a decision that is best for the patient at hand. At times, the weight of empirical evidence can seem so strong that it may seem we can effectively ignore other potential warrants for action, but to do so is to do the patient a disservice. To provide optimal care, clinicians must continue to use all of the medical knowledge and understanding at their disposal, recognizing the strengths and limitations of each. This understanding of clinical judgment has important implications for clinical medicine. First, since convincing warrants for action may come from within any of the 5 topics, empirical evidence, regardless of quality or quantity, will never be prescriptive. That is, the evidence never tells what we must do. In addition, the presumptive and individual nature of the conclusions anticipates and allows for variability of practice among clinicians. Clinical medicine remains, at its core, a personal and prudential discipline.

Table 2. Five Topics Relevant to Clinical Decision-Making

Empirical evidence	Derived from clinical research, including systematic reviews, randomized controlled trials, other controlled studies, and cohort studies
Experiential evidence	Derived from personal clinical experience or the clinical experience of others (experts)
Physiologic rationale	Applies an understanding of physiologic principles
Values	Includes patient and/or family goals and preferences, as well as professional values
System features	Includes economic, logistic, legal, and cultural facilitators or barriers to the provision of medical care. This topic is partly noted by Montori and Guyatt as "a sense of resource availability."[2] It certainly does not matter if low-stretch ventilation lowers mortality in ARDS if one does not have access to a ventilator

Summary

This discussion of the limits of EBM should not be interpreted as itself devaluing the importance of clinical research for clinical decision-making. The value of well-designed and well-conducted research is great, as one can see from reading the preceding articles in this (and the previous) issue of Respiratory Care. EBM, in attempting to define itself, has gradually come to recognize and acknowledge, to some degree, the value of alternative forms of medical knowledge and reasoning for clinical decision making. But by attempting to classify experiential knowledge and physiologic reasoning under the auspices of "evidence" and then relegating them to the realm of "lesser" evidence by promulgating arbitrary hierarchies, EBM fails to recognize that these forms of medical knowledge and reasoning remain important for bridging the necessary gap between research and practice. Empirical evidence, no matter the quality or quantity, even with the incorporation of patient values and preferences, will never be sufficient to determine optimal clinical practice. Clinicians must continue to muster all forms of medical knowledge at their disposal, weighing the relative importance of each with regard to the patient at hand, in order to come to the best decision for that individual.

REFERENCES

1. The Evidence-Based Medicine Working Group. Evidence-based medicine: a new approach to teaching the practice of medicine. JAMA 1992;268(17):2420–2425.

2. Montori M, Guyatt GH. What is evidence-based medicine and why should it be practiced? Respir Care 2001;46(11):1201–1214.
3. Grahame Smith D. Evidence based medicine: Socratic dissent. BMJ 1995;310(6987):1126–1127.
4. Horwitz RI. The dark side of evidence-based medicine. Cleve Clin J Med 1996;63(6):320–323.
5. Maynard A. Evidence-based medicine: an incomplete method for informing treatment choices. Lancet 1997;349(9045):126–128.
6. Naylor CD. Grey zones of clinical practice: some limits to evidence-based medicine. Lancet 1995;345(8953):840–842.
7. Feinstein AR, Horwitz RI. Problems in the "evidence" of "evidence-based medicine." Am J Med 1997;103(6):529–535.
8. Ellrodt G, Cook D, Lee J, Cho M, Hunt D, Weingarten S. Evidence-based disease management. JAMA 1997;278(20):1687–1692.
9. Tonelli MR. The philosophical limits of evidence-based medicine. Acad Med 1998;73(12):1234–1240.
10. Hess DR. The evidence for secretion clearance techniques. Respir Care 2001;46(11):1276–1292.
11. Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS. Evidence based medicine: what it is and what it isn't. BMJ 1996; 312(7023):71–72.
12. Reed E. The necessity of experience. New Haven: Yale University Press; 1996.
13. Sackett DL, Rosenberg WM. On the need for evidence-based medicine. Health Econ 1995;4(4):249–254.
14. Boyd NF, Sutherland HJ, Heasman KZ, Tritchler DL, Cummings BJ. Whose utilities for decision analysis? Med Decis Making 1990;10(1):58–67.
15. Pellegrino ED. The anatomy of clinical judgments. In: Engelhardt HT Jr, Spicker SF, Towers B, editors. Clinical judgment: a critical appraisal: proceedings of the Fifth Transdisciplinary Symposium on Philosophy and Medicine, held at Los Angeles, California, April 14–16, 1977. Boston: D Reidel Publ Co; 1979:169–174.

Discussion

Ellrodt: Mark, I would disagree with you on one thing, going back to the line [in author's slide presentation] that there is some evidence that distant prayer actually does improve outcomes.

Tonelli: There's a lot of good evidence about prayer and homeopathy; it's all floating out there. It's interesting and speaks to our unwillingness to necessarily become *highly* evidence-based on anything. That is, evidence is great, but it's got to fit with our biophysiologic model. It's got to fit with some other forms of understanding. But I like the distant prayer matrix. It's very hard to actually measure the quality of prayer, though, if somebody could come up with that.

Rowe: I'm very happy to hear, after looking at the title, that you entirely agree with Gordon Guyatt! I think that many of the people attending these sessions are believers. However, we also recognize that EBM has been abused, and like you say, if you put the term "evidence-based medicine" in the title of your article, you're increasing the likelihood of publication. A lot of work that *claims* to be evidence-based medicine is nothing *close* to evidence-based medicine. I think that if we realize that it's being misused, then that's a good thing and then we can restrict our comments to *true* evidence-based medicine. I think the reality is that what you're describing is essentially what EBM is moving toward. We're not minimizing patients' values. We're using the *best* evidence. It may not be a systematic review. It may not be a randomized, controlled trial. You've broken up experience into 3 areas: one is physiologic, one is experience, the other is system factors. I would argue that physicians or clinicians or whoever is making the decision with the patient is using all of those factors together in what we would consider "experience," and that the final decision for the patient is a combination of those 3 domains. So I don't think the people that propose evidence-based medicine are that far away from what you're describing.

Tonelli: I agree, and I hope that's true. I think one important distinction that we need to address is when we start talking about hierarchies of evidence, and when you throw some things into the evidence pool and leave some things out. We all understand empirical evidence, but if you label clinical experience and physiologic understanding as "evidence," and then you say we work on the *best* evidence, and the hierarchy is designed so that the best evidence comes from clinical research (what I call empirical evidence), it raises the question of whether the other stuff becomes unimportant once you have empirical evidence.

The hierarchies of evidence and practice guidelines go all the way through the types of empirical evidence and get to the conflicting, lousy studies, and below that they put expert opinion. Expert opinion! My argument here is that that's an experiential type of knowledge. It doesn't belong on that list of evidence at all. It's an entirely different kind of medical knowledge. So to some degree it's an important distinction. Are we talking about different kinds of medical knowledge? Because then hierarchies don't make sense. Are they different in kind or different in degree? Is evidence from randomized controlled trials always better than evidence from clinical experience? I think the answer is no. Sometimes clinical experience trumps the evidence from a randomized controlled trial, and sometimes arguing from physiologic rationale improves on your decision, relative to arguing strictly from the evidence. So there's that distinction, which I think is an important one, and I'm not sure what the evidence-based community has to say about that. They're fond of hierarchies.

I have absolutely no problem with a hierarchy of empirical evidence that stops when you stop talking about clin-

ical research. Once you start throwing in things thatare experiential, it becomes problematic.

The other thing is that I do think the evidence-based community bears some responsibility for the misinterpretations of EBM in that, if you don't talk about something, it implies you don't think it's important. When you say in an introduction to a textbook that integrating clinical experience and pathophysiologic rationale is important, and then nowhere else in the text do you discuss how to do that, or even discuss clinical experience, you're suggesting that maybe you don't think it's so important after all. I think that people are misunderstanding EBM when they say, "They devalue my 20 years of clinical experience, saying it's worth nothing." That's not what EBM proponents are saying. But they bear some responsibility for that misinterpretation. I welcome, and I think many people will, a discussion by EBM proponents about how that integration actually should happen.

Understanding Why We Agree on the Evidence but Disagree on the Medicine

Gordon D Rubenfeld MD MSc

Introduction
Clinical Decisions: Implicit or Explicit
From Evidence to Belief
From Belief to Decision
Understanding Conflicts When the Evidence Is Uncertain
A Concluding Proposal

Despite the fact that physicians, nurses, and respiratory therapists share a common training in scientific evidence and frequently share a common understanding of the evidence, debates occur about the proper management of individual patients. Clinicians may interpret this as a failure of evidence-based medicine, when, in fact, evidence is only one of many factors that play a role in clinical decision-making. By clearly understanding the other factors that affect clinical decision making—prior beliefs about treatment effectiveness, patient and clinician values, and clinical expertise—clinicians can better understand which clinical disagreements are about scientific evidence and which are about other factors. *Key words: evidence-based medicine, decision making, values, expertise, evidence.* [Respir Care 2001;46(12):1442–1449]

Introduction

A 19-year-old woman was involved in a high speed motor vehicle collision and sustained severe thoracic and skeletal trauma. Eighteen hours after admission she developed profound hypoxemic respiratory failure and was diagnosed with acute respiratory distress syndrome. Within several hours she was on 100% oxygen, high levels of positive end-expiratory pressure, and low-volume pressure-limited ventilation, and was paralyzed but continued to have frequent oxygen desaturations to 80%, associated with bradycardia. Two intensivists, equally familiar with the recent studies on therapy for acute respiratory distress syndrome met to discuss treatment options, including prone positioning, inhaled nitric oxide, and high-frequency oscillation. A vigorous debate ensued over the use of inhaled nitric oxide. Dr Advocate thought that inhaled nitric oxide was indicated and cited animal studies, the lack of a sufficiently ill subgroup in the clinical trials, and the basic physiologic fact that you cannot survive acute respiratory distress syndrome if you die of hypoxemia. Dr Skeptic pointed to the clinical trials showing lack of mortality benefit and the number of studies from cardiology and critical care that show that improving physiology does not necessarily improve survival. At one point, Dr Advocate accuses Dr Skeptic of being a slave to the evidence. Dr Skeptic responds by accusing Dr Advocate of not being a scientific physician.

Sometimes it is difficult to understand why there is any debate about evidence-based medicine (EBM). All medical, nursing, and allied health schools teach diagnosis and therapeutics grounded in the basic sciences of biochemistry, physiology, pharmacology, and microbiology. If medicine is not based on scientific evidence, then one won-

Gordon D Rubenfeld MD MSc is affiliated with the Division of Pulmonary and Critical Care Medicine, Harborview Medical Center, Seattle, Washington.

A version of this report was presented as the conference summary by Gordon D Rubenfeld MD MSc at the RESPIRATORY CARE Journal Conference, Evidence-Based Medicine in Respiratory Care, April 20–22, 2001, Banff, Alberta, Canada.

Correspondence: Gordon D Rubenfeld MD MSc, Division of Pulmonary and Critical Care Medicine, Harborview Medical Center, Box 359762, 325 9th Avenue, Seattle WA 98104. E-mail: nodrog@u.washington.edu.

ders. On what is it based? Debates about the value of EBM are expected between an allopathic physician and a Christian Science healer who bases her treatment recommendations on faith and the writings of Mary Baker Eddy, or between a physician and folk-based practitioners of traditional Chinese medicine, who base their treatments on collected experience passed along in written and oral form. However, as the proceedings of this Journal Conference indicate, debates about the appropriate role of EBM in everyday clinical decisions occur between clinicians who share similar scientific training.

As outlined by Guyatt in these proceedings and elsewhere, at least some of this debate is based on a misunderstanding of EBM.[1] Critics have argued, as Tonelli has in these proceedings, that EBM is flawed because evidence alone is never enough to direct a clinical decision.[2] There appears to be no disagreement between EBM advocates and their critics on this point.

> Evidence-based medicine is the conscientious, explicit, and judicious use of current best evidence in making decisions about the care of individual patients. The practice of EBM means integrating individual clinical expertise with the best available external clinical evidence from systematic research .... External clinical evidence can inform, but can never replace, individual clinical expertise, and it is this expertise that decides whether the external evidence applies to the individual patient at all ....[3]

Although that definition rescues EBM from the criticism that it ignores clinical judgment, it offers no definition of clinical expertise or practical advice on identifying expertise in ourselves or others.

Instead of addressing these philosophical concerns about the role of scientific evidence in medicine or the definition of clinical expertise, I would like to focus on more mundane questions—exemplified by the vignette at the beginning of this article—that occur daily in clinical medicine. Two excellent clinicians, each well acquainted with the scientific evidence about the diagnosis and management of a particular disease, each equally skilled in critical appraisal of the literature, and each equally likely to formulate an argument based on scientific evidence, disagree strongly. One would expect that a shared understanding of the evidence, of the proper role of evidence in informing medical decisions, and of the tools for evaluating the evidence would allow one clinician to convince the other of the optimal way to manage the case. Based on the definition of EBM, these disputes might be attributed simply to differences in clinical expertise: they disagree, quite simply, because one has better clinical judgment than the other. To know who is correct and whether it is appropriate to use a given treatment, we need only decide who has more clinical expertise. Besides the fact that this question is not particularly decidable, it fails to capture the depth of these conflicts, which are not solely due to differences in clinical judgment. If they were, then these debates would occur only at the bedside when specific patients were under consideration. In reality they occur in the editorial pages of our journals, at pro-con debates at our professional meetings, and in theoretical discussions about the value of treatments and diagnostic tests.

My goal is to explore the reasons evidence-based clinicians can and often do agree on the evidence but disagree on the medicine. This experience often leads clinicians to reject EBM as a failure when they disagree with a set of evidence-based guidelines, or when they disagree with a colleague who claims that his practice is evidence-based. I would like to provide clinicians with a road map to understand why, even when armed with the same critical literature appraisal skills and even after reading the same studies, Cochrane Reviews, and meta-analyses, clinicians find themselves disagreeing with a colleague or a guideline. The nature of these disagreements sheds light on our clinical decision process and on both the strengths and limitations of EBM.

Clinical Decisions: Implicit or Explicit

A great deal of clinical decision-making is influenced by factors that are rarely made explicit. Some unconscious factors like hunches and clinical intuition may be beneficial and contribute to clinical expertise. Unfortunately, cognitive psychology teaches us that many of these unconscious factors are detrimental to rational decision-making and include cognitive biases and rules of thumb.[4] The availability heuristic exaggerates the frequency of easily remembered, if rare, events and accounts for the drop in plane travel in the weeks after a major crash. The same unconscious bias may decrease a surgeon's threshold to operate in the weeks after a benign-appearing patient was sent home from the emergency room only to return with a burst appendix. We also tend to rely on simple rules-of-thumb; for example, the lesson received over an open abdomen during residency when an attending surgeon waved a normal appendix and said, "It's better to take out one hundred of these than to let even one burst!" That these factors influence our decisions is part of being human. That they influence our decisions without our being aware of them or able to discuss them reflects a lack of training. Requiring clinicians to justify the rationale for their decisions in explicit terms of probabilities and evidence is an essential aspect of EBM.

The extent to which medical decisions can be reduced to explicit probabilities, and the benefits of this style of decision-making, are old debates. To the ancient Greeks, medicine was an art (*tekne*) in the same category as archi-

tecture, painting, and metalsmithing. Even today much of medical training takes the form of apprenticeship: *see one, do one, teach one.* For years the art/science duality of medical practice has generated debate over the proper training and selection of clinicians.[5] Is something of the art of medicine lost when it is reduced to evidence, algorithms, and diagnostic technology? Is something of its humanity? Is EBM a threat to the professional integrity of clinicians?

The transformation is complete. My eyes
Are microscopes and cathode x-ray tubes
In one, so I can see bacteria,
Your underwear, and even through to bones.
My hands are hypodermic needles, touch
Turned into blood: I need to know your salts
And chemistries, a kind of intimacy
That won't bear pondering. It's more than love,
More weird than ESP—my mouth, for instance,
So small and sharp, a dry computer chip
That never gets to kiss or taste or tell
A brief truth like "You're beautiful," or worse,
"You're crying just like me; you are alive."[6]

When I went to the scientific doctor
I realised what a lust there was in him to wreak his
so-called science on me
and reduce me to the level of a thing.
So I said: Good-Morning! and left him.[7]

Attempts to make medical decisions explicit may strike some as intrinsically dehumanizing to the patient and clinician. Expecting the virtuosos of our profession to explain why they think a given test is indicated or how they reached their decisions may make them less special or reveal that they weren't special to begin with. Of course, the essential humanity of the clinician-patient relationship has more to do with communication skills, compassion, and trust than theories of medical decision-making. Fears that EBM and explicit decision-making will dehumanize medicine seem unfounded.

From Evidence to Belief

Before evidence can influence your practice, it has to change your belief. Every month our division hosts a Journal Club. A trainee presents a recent article from the medical literature and it is critically appraised. A vigorous discussion follows of the merits and limitations of the study. Eventually, the discussion slows and someone asks, "So do you believe this study? Will it change your practice?" After reading the same article and participating in the same discussion, it is surprising that opinions range from "absolutely not" through "probably not" and "I'll wait for the next study" to "I'd certainly consider it." Not too surprising is the fact that most of these opinions are the same as before they read the article and before they arrived at Journal Club.

When you read the results of a study, how much does the study change your belief?[8] This is a more complicated question than it appears and is influenced by 3 factors. Two of these, statistical confidence and study validity, are well known to readers of the scientific literature. Statistical confidence is expressed in the study result, its confidence interval, and associated p value. Studies with statistically significant results with narrow confidence intervals provide a great deal of statistical confidence. Unfortunately, statistical confidence is not very helpful if the study design was biased, flawed, invalid, did not include the right patient population, or did not deliver the therapy or diagnostic test correctly.

For example, an observational study showed with statistical confidence that pulmonary artery catheters were associated with increased mortality.[9] However, the study design could not completely eliminate the possibility that patients who received pulmonary artery catheters were sicker, and therefore this study has less effect on our beliefs than a study that could have addressed that issue. Evidence-based medicine provides an extensive set of tools to critically evaluate studies to assist readers in deciding how valid the studies are and how much they should influence our beliefs.[10] Although it is a simplification, a general hierarchy of study design is frequently cited that deems systematic reviews of multiple clinical trials the most valid and "expert opinion without explicit critical appraisal or based on physiology, bench research, or 'first principles'" the least valid.[11]

The importance of the third factor that affects believability is illustrated with a simple example. Homeopathic remedies are organic substances diluted in water to the point that there are few, if any, of the original molecules present in the treatment. A homeopathic remedy is so dilute that the standard theories of pharmacology and biophysics cannot explain any biologic activity. Contrary to conventional pharmacologic dose-response relationships, more dilute remedies are said to be more potent. Despite the obvious contradiction with standard pharmacology theory, patients all over the world use homeopathy every day; several well designed randomized double-blind clinical trials and at least one meta-analysis indicate the superiority of homeopathy to placebo.[12] Is the evidence-based clinician obliged to accept this high-level evidence of effectiveness and provide homeopathic remedies, discarding decades of accumulated knowledge about how molecules interact with living cells? Surely there are explanations for those positive trials: publication bias suppressed negative studies or chance alone caused the occasional positive study of an ineffective therapy. That may explain the homeopathy trials, but that is not the question. The question is,

Why are we more skeptical of this particular therapy than others in the face of evidence?

The answer is that we are all good Bayesian reasoners. Phrased somewhat intuitively, 18th century English mathematician Thomas Bayes showed that your evidence-based beliefs about the world are related to the strength of the evidence presented to you ("statistical confidence" and "validity" in the terms used in this essay; "likelihood ratio" or "likelihood function" in Bayesian terms) *and* the beliefs you had constructed based on available evidence before you learned the new evidence ("prior probability" or just "prior" in Bayesian terms).[13] So if I have a very strong belief that unicorns do not exist and you tell me you have one in your backyard, then seeing it through the window is not going to convince me that that single-horned animal is a unicorn, because that observation lacks sufficient validity (the likelihood ratio is not high enough). I will want stronger evidence. I may want to come over and pull on the horn or take a skull radiograph. Alternatively, if I have a strong prior that horses do exist and you tell me that you have one in your backyard, it won't take much to convince me that you've got one. I may even take your word for it. Similarly, if I have a strong prior that, generally speaking, biologic molecules must be physically present to exert an effect on cells, then it will take a very compelling body of evidence to convince me of the effectiveness of homeopathy. I will be inclined to believe that positive clinical trials are false positive trials and that negative trials have been suppressed. Contrast this with the minimal evidence it will take to convince me that a new modified cephalosporin antibiotic kills streptococci.

Bayesian reasoning is intuitive for clinicians, who implicitly or explicitly apply it every time we perform a diagnostic test. In this application we talk about prior probability of disease (beliefs you constructed before ordering the test), accuracy of the test (likelihood ratio of the test), and posterior probability of disease (strength of your new beliefs after the test results). We believe pulmonary angiograms more than ventilation-perfusion scans for the same reasons we believe randomized clinical trials more than case series. They both have higher likelihood ratios. If we really think someone has had a pulmonary embolism, a nearly normal ventilation-perfusion scan won't be enough evidence to convince us otherwise. If we agree with one clinical investigator who wrote that it "is hard to imagine that [inhaled nitric oxide] with such wide and consistent physiologic benefit cannot find a niche in adult medicine,"[14] then it may take many negative clinical trials to convince us that inhaled nitric oxide lacks clinical utility.

The Bayesian nature of scientific reasoning makes sense. New knowledge is discounted when unexpected, unless it is compelling in quality. Skeptics will criticize and acolytes will advocate until the evidence is sufficiently strong to bring consensus. Even at that point, there will be outliers with particularly strong priors that continue to criticize or advocate for a long time. How is this possible? Because scientific research rarely speaks with a single voice. No study can be interpreted in isolation and none is perfect. Techniques for combining evidence using meta-analysis are available, but even sophisticated meta-analysis techniques have problems incorporating variations in study quality, study populations, and study intervention. Even though there are accepted criteria to critically evaluate the study, there is always some aspect that a reader with a sufficiently strong prior can find to criticize. Consider the negative clinical trial. Skeptics of the treatment readily—perhaps too readily—accept it as evidence that the treatment is useless. Advocates raise the issues of lack of power, improperly delivered therapy, and incorrect patient population, and point to imbalances between the treatment and control groups.[15,16]

The effects of varied priors on levels of confidence in treatment decisions are not a problem when the likelihood ratio of the available evidence will overwhelm any prior; when, for example, there are dozens of consistent randomized clinical trials and multiple meta-analyses of various methodology yielding the same evidence of benefit or harm. It is nearly impossible, or at least irrational, to defend one's prior in the presence of that level of evidence. For example, there are few clinicians who doubt that aspirin or β blockade reduce mortality after myocardial infarction or that inhibiting angiotensin-converting enzyme prolongs survival in patients with congestive heart failure. On the other hand, consider the conclusions of a recent meta-analysis of total parenteral nutritional (TPN) in critical illness: "while TPN may have a positive effect on nutritional end points and on even minor complications, the overall results of our meta-analysis fail to support a benefit of TPN on mortality or major complication rates, particularly in critically ill patients."[17] With the exception of a dogmatic stance that TPN must be provided to save lives in the critically ill, that meta-analysis could support a range of clinical opinions about the use of TPN, depending on one's assessment of its risks and the value of "nutritional end points."

From Belief to Decision

Decisions involve much more than beliefs about the evidence of effectiveness of treatments or diagnostic tests. As noted previously, decisions involve assessing whether the available data apply to a particular patient. For example, are the data from a clinical trial showing benefits from a lung-protective ventilator strategy in acute respiratory distress syndrome applicable to patients with cirrhosis even though they were excluded from the trial? Are the mechanism of the treatment and the pathophysiology of cirrho-

sis such that lung-protective ventilation is unlikely to be effective or more likely to be harmful in cirrhotic patients? Does the lack of efficacy of inhaled nitric oxide in a broad population of adults with acute respiratory distress syndrome preclude its efficacy as salvage therapy in a subset? This is a fascinating source of clinical disagreement, whose explication would involve a detailed understanding of what we mean by clinical expertise and application of population data to individual patients. Given the central role clinical expertise has in EBM, it seems a fruitful area for research.

An equally important step in making a clinical decision is assessing the patient's values (see Table 1). Regardless of the evidence supporting the use of anticoagulation for chronic atrial fibrillation, a patient who would rather have a stroke than give up her cherished hobby of rock climbing should not receive Coumadin. Regardless of whether surgical therapy for prostate cancer prolongs survival, a man who would rather die than risk impotency or incontinence should not have the operation. Though assessing and incorporating these values are part of EBM, as they are part of any medical care that seeks informed consent, these values themselves are not evidence-based. Values come from many places, and though physicians may be tempted to say "no one should value independence over a stroke," the only evidence that is relevant is the ability to express the various risks of different outcomes to patients in ways they understand. Although there is compelling evidence that we do a terrible job at this step of clinical decision making, I think all clinicians appreciate, in theory, its importance. What clinicians may fail to appreciate is the important role *their own* values play in clinical decisions.

Many patients might be surprised to learn that their physician's age, religious practices, where he or she trained, and various other personality factors have a strong influence on clinical decisions.[18-20] Physicians, like their patients, have values about various outcomes and processes of care. These have been somewhat less well studied than patients' preferences (Table 2). Modern medical ethics' emphasis on patient autonomy teaches that competent patients' values should dominate the values decisions at stake, with the possible exception of justice, which, although presented in Table 2 as a clinician value, is likely to be shared by clinicians and patients. Evidence-based medicine accepts and even emphasizes the important role of patient values. However, the proper role of clinician values in decision-making is not as clear. Can a clinician's value to avoid a malpractice claim justify defensive laboratory testing when the evidence indicates that positive results are more likely to represent false positives than true disease? Can a clinician's value for justice justify withholding an expensive, potentially effective therapy when there is no mechanism to ensure that the money saved will be redistributed to provide more cost-effective therapies? It is less important to provide convincing answers to these questions than it is to recognize what forces are influencing our choices.

Understanding Conflicts When the Evidence Is Uncertain

A number of clinician-specific factors—clinical expertise, decision-making style, prior beliefs in treatment efficacy, patient values, and clinician values—all influence the translation of evidence into a clinical decision. Given individual variability in all of those factors, it is surprising that we ever actually agree on patient management. When the evidence is robust, when there is clear and consistent evidence of superiority of a therapy, and when the risks and benefits of the treatment in multiple patient subgroups are known, disagreements tend to collapse to an assessment of patient values. As the proceedings of this Journal Conference indicate, this surfeit of evidence is a luxury not enjoyed by pulmonary medicine and particularly rarely encountered in critical care. This is not to say that pulmonary and critical care medicine lacks evidence. Many therapies, including antibiotics for infections, fluid for hypovolemic shock, ventilatory support for respiratory failure, and β agonists for acute asthma, fall into the strong category of "all or none" evidence where benefit is presumed, as controlled trials would be unethical.

Unfortunately, we are often faced with treatment decisions when the evidence base is less than compelling. There appears to be no consensus on how best to synthesize the evidence into a single statement of "best available evidence."[25] For example, the best available evidence may only preclude emphatic claims of benefit or harm when it shows no randomized clinical trials or only small trials of

Table 1. Examples of Patient Values Affecting Clinical Decisions

Value	Definition	Example
Quality of life	Patient prefers quality of life to a prolongation of life	Decision to forego aggressive chemotherapy for advanced cancer
Fear of specific complication	Patient weights certain complications and outcomes differently than others	Fear of breast cancer over heart disease influences woman's choice about hormone replacement therapy
Cost	Personal or family risk of financial burden influences therapy	Decision to use generic medication 3 times per day instead of a more expensive medication once a day

Table 2. Examples of Clinician Values Affecting Clinical Decisions

Value	Definition	Examples
Primum non nocere	First do no harm. Doctor causing harm is worse than other adverse outcomes	The decision not to place pulmonary artery catheters until evidence of benefit[21]
Chagrin	Overtreating and test ordering are less likely to result in embarrassing missed complications and missed diagnoses[22]	The decision to prescribe antibiotics to an elderly patient with a viral syndrome
Rescue	Imminent death justifies heroic interventions[23]	The decision to use inhaled nitric oxide in the vignette at the beginning of this report
Justice	Costs and benefits should be distributed equitably in society	The decision *not* to use inhaled nitric oxide in the opening vignette at the beginning of this report
Fear	Fear of litigation	The decision to perform a cesarean section[24]

poor quality; or when a meta-analysis concludes that there is no evidence of benefit (or harm), but the confidence interval around the treatment effect spans important potential benefit; or when different meta-analyses reach different conclusions; or when the clinical trials have studied such different treatments or patient populations that a meta-analysis is uninterpretable; or when observational and laboratory data are compelling and available clinical trial data are limited and negative.

Avoiding emphatic claims of benefit leaves a lot of room for clinical expertise, decision-making style, priors, and clinician values to dominate the debate. Nevertheless, consensus panels, insurance companies, and individual clinicians arrive at evidence-based recommendations. Sometimes they arrive at recommendations that conflict.[26–28] Evidence-based guidelines certainly use different language to phrase the strength of their recommendations (Table 3).

I have argued that to reach recommendations or decisions, individual clinicians and consensus panels must, implicitly or explicitly, incorporate prior probabilities and values. When EBM is working particularly well, this process is explicit and the reader can separate the evidence synthesis from the process that turns it into a decision or recommendation.[31] Unfortunately, these completely distinct processes, evidence synthesis (assembly of best available evidence) and evidence-based recommendation (incorporation of values, risks, benefits, prior beliefs, etc), are sometimes conflated. It is essential that the incorporation of these external (ie, external to the evidence) factors are incorporated explicitly in such a way that readers can separate the evidence from the process by which the evidence is turned into a decision. Egregious violations occur. In a Cochrane review entitled "Colloids Versus Crystalloids for Fluid Resuscitation in Critically Ill Patients," the authors concluded that "There is no evidence from randomized controlled trials that resuscitation with colloids reduces the risk of death compared to crystalloids in patients with trauma, burns, and following surgery," which is their summary of the available evidence.[32] The next sentence reads, "As colloids are not associated with an improvement in survival, and as they are more expensive than crystalloids, it is hard to see how their continued use in these patient types can be justified outside the context of randomized controlled trials." Though that conclusion may be "based" on the evidence, it incorporates strong values about cost-effectiveness that are nowhere present in the clinical trials of fluid resuscitation.

A Concluding Proposal

Evidence-based medicine is a misleading term because it implies that evidence-based practice recommendations are solely based on evidence. In fact, EBM specifically acknowledges the role of patient values and clinical expertise, so "evidence-, expertise-, and value-based medicine" would be a more accurate but less appealing name. Evidence-based medicine is a divisive term because it implies that clinicians who deviate from "evidence-based" recommendations are practicing some other form of medicine, despite following an EBM process to arrive at their decisions.

This process of breaking down a decision into answerable pieces and assigning explicit probabilities and utilities to the outcomes using the best available evidence is not new, did not start in medicine, and precedes EBM by at least 20 years. Decision analysis is a derivative of game theory, developed and applied in business and economics since the 1940s. It is a "systematic quantitative approach for assessing the relative value of one or more different decision options" that includes (1) identifying a relevant clinical problem, (2) breaking the problem down into a tree of different potential outcomes, (3) using the best available evidence to assign probabilities to those outcomes, and (4) assigning values or utilities to the outcomes based on patient, clinician, and societal values.[33] Step 3 involves the same rigorous search for best available evidence, systematic reviews, and meta-analyses used in EBM. In fact, the processes of EBM and applied decision analysis seem nearly identical to me. Decision analysis has several advantages over the process described as EBM. The separation of empirical facts ("best available evidence") from clinician, societal, and patient values is much more explicit than EBM and makes a clear separation of

Table 3. Schemes for Grading Evidence-Based Recommendations

Oxford Centre for Evidence-Based Medicine, Grades of Recommendations[11]	Global Obstructive Lung Disease Guidelines[29]	*British Medical Journal, Clinical Evidence*[30]		Guidelines for Antithrombotic Therapy[31]
A Consistent Level 1 studies	A Randomized clinical trials; rich body of data	Beneficial	Interventions whose effectiveness has been established by clear evidence from randomized controlled trials, and expectation of harms that is small compared to the benefits.	1A Randomized trials without important limitations. Strong recommendation; can apply to most patients in most circumstances, without reservation.
B Consistent Level 2 or 3 studies or extrapolations from Level 1 studies	B Randomized clinical trials; limited body of data	Likely to be beneficial	Interventions for which effectiveness is less well established than for those listed under "beneficial."	1B Randomized trials with important limitations (inconsistent results, methodologic flaws). Strong recommendation; likely to apply to most patients.
C Level 4 studies or extrapolations from Level 2 or 3 studies	C Nonrandomized trials; observational studies	Trade-off between benefits and harms	Interventions for which clinicians and patients should weigh the beneficial and harmful effects, according to individual circumstances and priorities.	1C+ No randomized controlled trials, but randomized controlled trial results can be unequivocally extrapolated, or overwhelming evidence from observation studies. Strong recommendation; can apply to most patients in most circumstances.
D Level 5 evidence or troublingly inconsistent or inconclusive studies of any level	D Panel judgment consensus	Unknown effectiveness	Interventions for which there are currently insufficient data or data of inadequate quality (includes interventions that are widely accepted as beneficial but have never been formally tested in randomized controlled trials, often because randomized controlled trials would be considered unethical).	1C Observation studies. Intermediate-strength recommendation; may change when stronger evidence available. 2A Randomized trials without important limitations. Intermediate-strength recommendation; best action may differ, depending on circumstances or patient's or societal values.
		Unlikely to be beneficial	Interventions for which lack of effectiveness is less well established than for those listed under "likely to be ineffective or harmful."	2B Randomized trials with important limitations (inconsistent results, methodologic flaws). Weak recommendation; alternative approaches likely to be better for some patients under some circumstances.
		Likely to be ineffective or harmful	Interventions whose ineffectiveness or harmfulness has been established by clear evidence.	2C Observation studies. Very weak recommendation; other alternatives may be equally reasonable.

the evidence synthesis from the decision. Since an important goal of EBM is explicitness, this seems an advantage. Decision analysis also can convey uncertainty by using sensitivity analysis, which allows the user to see the effects of assuming that the treatment is really twice as effective as the available data suggest. This distinction is important because resolution of clinical debates like those in the opening vignette require clinicians to distinguish between arguments over interpretation of the evidence and disagreements over clinical expertise, prior assumptions about benefits, uncertainty, or an individual clinician's complex set of clinical values.

REFERENCES

1. Guyatt GH, Haynes RB, Jaeschke RZ, Cook DJ, Green L, Naylor CD, et al. Users' guides to the medical literature: XXV. Evidence-based medicine: principles for applying the users' guides to patient care. Evidence-Based Medicine Working Group. JAMA 2000; 284(10):1290–1296.
2. Tonelli MR. The philosophical limits of evidence-based medicine. Acad Med 1998;73(12):1234–1240.
3. Sackett DL, Rosenberg WM, Gray JA, Haynes RB, Richardson WS. Evidence based medicine: what it is and what it isn't. BMJ 1996; 312(7023):71–72.
4. Kahneman D, Slovic P, Tversky A. Judgment under uncertainty: heuristics and biases. Cambridge: Cambridge University Press; 1987.
5. Thomas L. The youngest science: notes of a medicine-watcher. Boston: GK Hall; 1983.
6. Campo R. The other man was me: a voyage to the new world. Houston: Arte Público Press; 1994. (Reprinted with permission)
7. Lawrence D H, Pinto VDS, Roberts W. The complete poems of DH Lawrence. New York: Penguin Books; 1977.
8. Browner WS, Newman TB. Are all significant p values created equal? The analogy between diagnostic tests and clinical research. JAMA 1987;257(18):2459–2463.
9. Connors AF Jr, Speroff T, Dawson NV, Thomas C, Harrell FE Jr, Wagner D, et al. The effectiveness of right heart catheterization in the initial care of critically ill patients. Support Investigators. JAMA 1996;276(11):889–897.
10. Guyatt GH, Rennie D. Users' guides to the medical literature. JAMA 1993;270(17):2096–2097.
11. Oxford centre for evidence-based medicine levels of evidence. http://cebm.jr2.ox.ac.uk/docs/levels.html.
12. Linde K, Clausius N, Ramirez G, Melchart D, Eitel F, Hedges LV, Jonas WB. Are the clinical effects of homeopathy placebo effects? A meta-analysis of placebo-controlled trials. Lancet 1997;350(9081): 834–843.
13. Howson C, Urbach P. Scientific reasoning: the Bayesian approach, 2nd ed. Chicago: Open Court; 1993.
14. Dellinger RP. Inhaled nitric oxide in acute lung injury and acute respiratory distress syndrome: inability to translate physiologic benefit to clinical outcome benefit in adult clinical trials. Intensive Care Med 1999;25(9):881–883.
15. Zapol WM. Nitric oxide inhalation in acute respiratory distress syndrome: it works, but can we prove it? Crit Care Med 1998;26(1):2–3.
16. Matthay MA, Pittet JF, Jayr C. Just say NO to inhaled nitric oxide for the acute respiratory distress syndrome. Crit Care Med 1998;26(1): 1–2.
17. Heyland DK, MacDonald S, Keefe L, Drover JW. Total parenteral nutrition in the critically ill patient: a meta- analysis. JAMA 1998; 280(23):2013–2019.
18. Christakis NA, Asch DA. Biases in how physicians choose to withdraw life support. Lancet 1993;342(8872):642–646.
19. Christakis NA, Asch DA. Physician characteristics associated with decisions to withdraw life support. Am J Public Health 1995;85(3): 367–372.
20. Cook DJ, Guyatt GH, Jaeschke R, Reeve J, Spanier A, King D, et al. Determinants in Canadian health care workers of the decision to withdraw life support from the critically ill. JAMA 1995;273(9): 703–708.
21. Robin ED. Death by pulmonary artery flow-directed catheter: time for a moratorium? Chest 1987;92(4):727–731.
22. Feinstein AR. The 'chagrin factor' and qualitative decision analysis. Arch Intern Med 1985;145(7):1257–1259.
23. Hadorn DC. Setting health care priorities in Oregon. cost-effectiveness meets the rule of rescue. JAMA 1991;265(17):2218–2225.
24. Tussing AD, Wojtowycz MA. Malpractice, defensive medicine, and obstetric behavior. Med Care 1997;35(2):172–191.
25. Concato J, Shah N, Horwitz RI. Randomized, controlled trials, observational studies, and the hierarchy of research designs. N Engl J Med 2000;342(25):1887–1892.
26. Niederman MS, Bass JB Jr, Campbell GD, Fein AM, Grossman RF, Mandell LA, et al. Guidelines for the initial management of adults with community-acquired pneumonia: diagnosis, assessment of severity, and initial antimicrobial therapy. American Thoracic Society. Medical Section of the American Lung Association. Am Rev Respir Dis 1993;148(5):1418–1426.
27. Bartlett JG, Dowell SF, Mandell LA, File TM Jr, Musher DM, Fine MJ. Practice guidelines for the management of community-acquired pneumonia in adults. Infectious Diseases Society of America. Clin Infect Dis 2000;31(2):347–382.
28. Mandell LA. Guidelines for community-acquired pneumonia: a tale of 2 countries. Clin Infect Dis 2000;31(2):422–425.
29. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease. NHLBI/WHO workshop. http://www.goldcopd.com. Accessed Sept 25, 2001.
30. Categorisation of treatment effects in clinical evidence. http://www.clinicalevidence.org/. Accessed Sept 25, 2001.
31. Guyatt G, Schunemann H, Cook D, Jaeschke R, Pauker S, Bucher H. Grades of recommendation for antithrombotic agents. Chest 2001; 119(1 Suppl):3S–7S.
32. Alderson P, Schierhout G, Roberts I, Bunn F. Colloids versus crystalloids for fluid resuscitation in critically ill patients (Cochrane Review). In: The Cochrane Library, 3, 2001. Oxford: Update Software.
33. Petitti DB. Meta-analysis, decision analysis, and cost-effectiveness analysis: methods. New York: Oxford University Press; 1994.

Reviews of Books and Other Media. Note to publishers: Send review copies of books, films, tapes, and software to RESPIRATORY CARE, 600 Ninth Avenue, Suite 702, Seattle WA 98104.

Books, Films, Tapes, & Software

Users' Guide to the Medical Literature: A Manual for Evidence-Based Clinical Practice. The Evidence-Based Medicine Working Group. Gordon Guyatt MD and Drummond Rennie MD, editors. Chicago: AMA Press. 2002. Soft-cover, 706 pages (with CD-ROM and pocket memory aides), $49.95.

Users' Guides to the Medical Literature: Essentials of Evidence-Based Clinical Practice. The Evidence-Based Medicine Working Group, Gordon Guyatt MD and Drummond Rennie MD, editors. Chicago: AMA Press. 2002. Soft cover, 442 pages (with CD-ROM and pocket memory aides), $34.95

Over the past several years, students, residents, and faculty in my courses on critical appraisal of the literature and evidence-based medicine (EBM) have consistently asked, "Has anybody put all the *Users' Guides to the Medical Literature* series into a single resource?" Until now, the answer has always been no. The authors of that series, which has been appearing in the *Journal of the American Medical Association* since 1993, have answered those learners' requests with these 2 books, the **Manual** and the **Essentials**. The books are intended for clinicians who wish to understand how to evaluate the validity of the published literature and then apply it to the care of patients. The **Manual** is intended for those who desire more in-depth information and for those who teach EBM, whereas the **Essentials** is intended for those whose needs are less detailed, such as learners and most practitioners. Though the books are filled with clinical scenarios and examples from the medical literature that reflect traditional medical problems, the principles apply to any discipline.

More than a mere compilation of the original articles, which provided a "how to" primer on evaluating the validity of published research, these books provided the authors an opportunity to address their philosophy, to address some of the criticisms of EBM, and to synthesize their material into a homogeneous work. They have clarified areas that are common misperceptions of EBM. In particular, their discussion about the importance of patient values in clinical decision-making is perhaps their strongest yet ("Evidence Is Never Enough").

The books are well organized and the information is presented in a clear and easy-to-understand style. The **Manual** has 2 parts. Part 1 summarizes the basics of using the medical literature. Part 2 is more advanced, focusing on a more sophisticated level of understanding and on those who teach. The **Essentials** is a concise summary of the **Manual**, sharing the same organizational framework but providing much less content in Part 2. At the end of each book is an appendix with formulas for calculating important numbers, and a glossary of terms. Each book comes with a CD-ROM (containing the full text of the **Manual**) and 4 pocket-sized memory aids.

Part 1 begins with the philosophy of EBM, followed by a chapter on finding the evidence. These are followed by chapters on therapy and harm, diagnosis, prognosis, summarizing the evidence, and moving from evidence to action. The editors chose an unusual method for numbering the chapters and chapter sections. Chapters in Part 1 begin with the number 1 followed by a letter. The authors use a parallel structure in Part 2. For instance, the first chapter in Part 1, on the philosophy of EBM, is labeled 1A. The corresponding expanded content in Part 2 is labeled 2A. This works, except sections in one part don't always have corresponding content in the other. For example, "1A1 Finding the Evidence" has no corresponding content in Part 2, and "2B3 Therapy and Applying the Results" has no corresponding Part 1 content. These might confuse the reader.

The CD-ROM included with each book has the complete text of the **Manual**. The installation routine is simple and quick. It installs Adobe Acrobat Reader version 5 and the corresponding portable display format ("pdf") files. For those installing the CD-ROM onto IBM-compatible systems, the **Manual** has a rich set of hyperlinks to facilitate the reader's experience. Hypertext links take the reader to pop-up windows (glossary items, references, annotations) or to other sections of the book. Closing the pop-up window or hitting the "back arrow" allows the reader to continue from the previous section. Those readers using Apple computers can only use the CD-ROM as a read-only file that lacks the hypertext features.

The index is reasonably easy to use, but there are some idiosyncrasies. For instance, to find content about "guidelines" one needs to look for "clinical practice guidelines." Though that is forgivable, the CD version suffers from the same deficiency. Typing in the word "guideline" under the search tab of the index results in 36 items, yet using the plural yields 192. One can limit the search to titles (yields only 1 item). To narrow the search, one can also perform additional searches on the previous search.

In Part 1, the authors include relatively new material addressing the utility of "predigested" critical summaries of the literature. This may surprise some readers, as it represents a departure from their longstanding focus. Part 1 also includes discussion on the strength of evidence about therapeutic interventions, which may surprise the casual reader of the EBM literature: the strongest evidence about the benefit of a therapeutic intervention for an individual patient comes from an n of 1 trial with that patient. The corresponding tutorial in Part 2 provides the simplest and clearest explanation of how to conduct and evaluate the results of such a trial. This latter content is not included in the **Essentials**, but it is included on the CD-ROM.

The authors (appropriately) focus heavily on the content that most directly affects clinical decision-making: making a diagnosis, assessing risk, establishing prognosis, and therapy and harm. The clinical scenarios and references facilitate the reader's understanding of difficult concepts. The references are current and accurate, and the examples include women, children, medicine, and surgery.

It is difficult to criticize a group that for the past 20 years has made great contributions in the critical appraisal of the medical literature. Nonetheless, there are a few areas that need work. The books' primary focus is on how to critically appraise the validity of primary research articles, and they easily address that focus. However, the underlying assumption that practitioners can or should do their own critical reading is not fully addressed. The approach to EBM espoused

by Shaughnessy and Slawson[1-3] is completely ignored in the **Essentials** and the **Manual**. Shaughnessy and Slawson begin with the question, "If this information is valid, would it require me to change my practice?" They encourage decision-makers to look for information sources that validate and summarize research.

The authors of the **Essentials** and the **Manual** also address the latter point and present a table summarizing some reliable sources of such information. However, the table is incomplete, and they don't describe the criteria they used to decide which sources were included. Though it is unusual for chapter authors and book editors to disclose potential conflicts of interest, this table deserves such disclosure (if conflict exists), since several of the resources are proprietary.

One other point of criticism also occurs at the outset. Obviously patient preferences are extremely important in clinical decision making, but the discussion of this subject in Part I (of both books) is cursory. Though it is more fully explored in Part 2 of the **Manual**, it is not in the **Essentials**. As a potential source of motivation for the skeptics and for the beginner, shared decision-making deserves more attention in the introductory chapter. Additional discussion about patient-provider communication and the format of information transfer would have been helpful.

Criticisms aside, these books serve as an important source of "how to" for the individual to learn how to critically appraise the medical literature and as a resource for the teacher of EBM. One of these books should be in the personal library of anyone interested in EBM. The only reason I can think to own both volumes is for the course director who needs both to assist in developing and coordinating course assignments. Frankly, if forced to make a choice, I'd spend the extra money for the **Manual**. This would allow the reader to access all the advanced material without having to read from a computer screen.

Henry C Barry MD
Department of Family Practice
Michigan State University
East Lansing, Michigan

REFERENCES

1. Slawson DC, Shaughnessy AF, Bennett JH. Becoming a medical information master: feeling good about not knowing everything. J Fam Pract 1994;38(5):505–513.
2. Shaughnessy AF, Slawson DC, Bennett JH. Becoming an information master: a guidebook to the medical information jungle. J Fam Pract 1994;39(5):489–499.
3. Slawson DC, Shaughnessy AF. What clinical information do doctors need? Few doctors are expert at evaluating information. BMJ 1997;314(7084):904.

Studying a Study and Testing a Test: How to Read the Medical Evidence, 4th edition. Richard K Riegelman MD MPH PhD. Philadelphia: Lippincott Williams & Wilkins, 2000. Soft cover (with CD-ROM), illustrated, 536 pages, $39.95.

The medical literature is continuously increasing in quantity, presentation, and specialization. At the same time, practitioners are facing increasing pressure to make decisions based on the evidence presented within that literature. With each passing day the task becomes more formidable. The volume of material has increased dramatically. There are more manuscripts being published and more journals within which to publish them. These journals are quite disparate. Some cover very broad topics with relevance to many areas of health care, and others are highly specialized, covering topics with relatively few followers. In years past, the print media and conferences were the only venues to present research findings and clinical reports. Now with the emergence of electronic media there is a huge amount of opportunity for expansion of the peer-reviewed literature.

For many, the ability to analyze scientific material was learned in a college or graduate school statistics course. For others, the learning was "on the job" and passed down from mentors. Richard Riegelman has provided a systematic "how to" approach to interpreting the medical literature for the current generation of practitioners. **Studying a Study and Testing a Test**, now in its fourth edition, has become a required component of the personal library of physicians, nurses, therapists, and researchers alike, who need the tools to critically review medical reports. Because the book is well organized, it serves readers well as a core textbook for a graduate level statistics or epidemiology class. Alternatively, it provides a self-study module for practitioners who are interested in improving their knowledge of interpreting the medical literature.

In Part I, Riegelman provides the foundation for "Studying a Study." He describes the "universal framework" conceptual approach to evaluating health studies. In a stepwise manner, critical elements of a study's design, patient assignment, outcome determination, analysis, and interpretation are covered. The section covers everything from the explicit statement of the study's hypothesis to the extrapolation of the findings to different populations, and includes warnings that threaten a study's validity, such as bias, confounding, and inadequate power. The remaining parts of this section demonstrate the application of the universal framework to different study designs, the randomized controlled trial, the nonconcurrent cohort study, and the meta-analysis. Chapter 12 (and the last chapter of each section) provides a bullet-format summary that allows for ease of reference and the ever-present "flaw-catching exercises" that allow the reader to apply the newly acquired knowledge.

Part 2, entitled "Testing a Test," provides the reader with an understanding of the imperfections in tests that arise because of variability in the subject being tested, the test itself, or the observer. Riegelman then helps the reader to refine this knowledge by presenting sensitivity, specificity, positive and negative predictive value, and the use of tests for screening.

Part 3, "Rating a Rate," introduces the concepts of rates, proportions, and rate standardization. Change in rates and real versus artifactual differences are discussed next. Finally, the author demonstrates the application of the material to the problem of life expectancy.

Part 4, "Considering Costs and Evaluating Effectiveness," is a new section in this fourth edition. The section begins with how studies can be used for decision-making purposes. The universal framework is again invoked to help analyze studies designed for a decision-making purpose. Along the way, the reader acquires an introduction to the vocabulary associated with these investigations. For example, cost effectiveness, quality-adjusted life expectancy, utility, and discounting are all discussed. The author makes liberal use of decision trees that enhance the reader's ability to integrate the concepts with the mathematics.

The final section, "Selecting a Statistic," helps the reader understand categories of data and select a statistic based on the number of variables that need to be considered in an analysis. Again, the liberal use of flow charts provides the reader with a visual fig-

ure that can be referred to repeatedly to find the appropriate statistical test to use.

The book has universal appeal to practitioners with a range of education and experience because the material is progressively presented, providing basic information followed by more elaborate discussion of advanced topics. The beginner is never overwhelmed. The accompanying CD-ROM provides additional questions with answers and justification that can be taken for continuing medical education credit. The glossary included both in the text and on the CD-ROM is similarly extensive and functions as a valuable reference for unfamiliar statistical and epidemiologic terms as the reader works through the more difficult sections of the text. The medical literature will continue to expand beyond our ability to integrate it successfully into our practice. But **Studying a Study and Testing a Test** will provide all practitioners, regardless of their discipline or training, with the background necessary to critically evaluate and understand the medical evidence.

Anthony D Slonim MD
Critical Care Medicine
Children's National Medical Center
Departments of Pediatrics and
Internal Medicine
The George Washington University
School of Medicine
Washington DC

Evidence-Based Clinical Practice: Concepts and Approaches. John P Geyman MD, Richard A Deyo MD MPH, and Scott D Ramsey MD PhD, editors. Boston: Butterworth-Heinemann. 2000. Soft cover, illustrated, 177 pages, $37.50.

At one point in this monograph the authors note that the widespread adoption of evidence-based medicine (EBM) may have a more profound effect on clinical medicine and patient outcomes than the results of the Human Genome Project. Eight years after the first publication of the *User's Guides to the Medical Literature*,[1] however, most clinicians still struggle with the application of medical literature to their daily clinical problems. Moving to the new paradigm of EBM is a difficult process, since most of us trained, and continue to train, in institutions where approaches to clinical problems using pathophysiologic reasoning and the easy availability of experts predominate. This book is a pleasant introduction to the process, which is intended to acquaint readers with the concepts and practical implications of the growing field of EBM.

The stated target audience is primary care physicians, residents, fellows, medical students, and other decision-makers in the delivery of primary care, but it is well-suited to any health care professional who is interested in improving his or her use of the medical literature in clinical practice. The book's length and readability make it ideal for busy clinicians; most of the chapters are 10 pages or less. I found some of the conceptual discussions a bit brief for early learners and for that reason would not recommend it to medical students.

The aims of the book, presented in the preface, are to:

- Introduce clinicians to evidence-based medicine as part of clinical decision making
- Enable clinicians to more critically read the literature and develop new skills of self-learning
- Prepare clinicians and other decision makers in health care to better evaluate clinical guidelines
- Elucidate complementary roles of clinical judgment and evidence-based approaches in individual practice settings
- Acquaint readers with techniques and limitations of cost and outcomes assessment
- Where appropriate, extend evidence-based approaches beyond the care of individuals, to populations being served

This is an ambitious agenda for less than 200 pages. The reader is left with a clear vision of the process of EBM—that is, reflecting on clinical situations encountered, asking questions, searching for answers, evaluating the literature. Whether skill development in each of these steps can occur with such brief descriptors is problematic, however.

The book is based on the monthly interdisciplinary Evidence-Based Clinical Practice Rounds at the University of Washington and edited by 3 well-known proponents and teachers of EBM. Several chapters have been reprinted from previously published articles, and their failure to recognize other chapters makes the flow of the book repetitive and choppy at times. For instance, a discussion of using computers in answering clinical questions in Chapter 17 has a table of Web-based resources that is almost identical to a table in Chapter 1, "Sources of High-Quality Evidence." Another chapter mentions the time trade-off method of determining patient preference, without referring to an earlier chapter in which it is defined. The chapters discussing outcomes research and patient preference between chapters discussing critical appraisal seemed out of place.

There is a clear effort, however, to link the concepts to clinical practice, and most chapters begin with a clinical scenario. Although these scenarios are drawn from primary care, they will be easily recognizable and transferable to other fields, such as pulmonary medicine.

The book opens with 2 chapters that define EBM and then present compelling examples of the need for it. The review of medical mythology taught in medical school, and how clinical studies have refuted many common clinical practices, was a particularly enjoyable read, and it motivates the reader to tackle the chapters that follow.

Chapter 4 is a quick introduction to searching MEDLINE and other EBM resources, such as the Cochrane database. It starts with suggestions for Internet connections, and includes a step-by-step description of a MEDLINE search on a clinical problem. There are several helpful pearls in this chapter, which will be useful to anyone beginning to access information on-line. Somewhat disappointing was the fuzzy quality of the figures depicting computer screens.

Chapters 5 and 6 address the second aim of the book, to enable readers to critically read the literature. Chapter 5 is a distillation of the McMaster University Evidence-Based Clinical Practice Working Group's guides and, after a discussion of the major categories of primary research and preferred study designs for particular questions, it presents the McMaster worksheets in accompanying tables. The tables are clear and will be a helpful reference. The chapter walks through an analysis of a published study using a worksheet. It would have been helpful to have this paper included in the text; readers should probably pull it and keep it at hand when working through the chapter. Similarly the chapter on meta-analysis presents a series of queries the clinician can use in making a decision on using results of a published meta-analysis.

The next chapter discusses the need for outcomes research, giving examples of generic as well as disease-related quality-of-life questionnaires, and pointing out the pitfalls in this type of research.

The chapter on measuring patient preference was the most difficult for me. The author initially emphasized his intent to focus on individual patient preferences that

would be important in clinical encounters, but then discussed measurement methodology in research studies, which was somewhat technical, and seemed fraught with error. Finally, the chapter returned to the importance of eliciting patient preference in individual clinical encounters. It was not clear to me that the methodology discussed applies to clinical practice. These concepts are important, however, in the later chapters that address decision analysis and cost-effectiveness studies.

Chapter 9, "Assessing the Accuracy of Diagnostic and Screening Tests," succinctly covered the major concepts of that subject. For novices to this material, however, there was insufficient explanation of likelihood ratios and rather oblique references to Bayes's theorem. Similarly the chapter on decision analysis was limited by an inadequate figure that did not follow the text, by lack of a discussion of how probabilities are obtained, and by limited description of the fold back process.

The chapters on cost-effectiveness research and the use of balance sheets in clinical practice guidelines were extremely well written and practical. The latter discussion envisions the clinicians as active participants in the construction of clinical practice guidelines, rather than as passive practitioners. Any health care professional asked to participate in developing a practice guideline will find this approach appealing.

Chapter 15 moves beyond the primary research to the use of systematic reviews. It includes a clear discussion of the concepts of relative risk, absolute risk, and number needed to treat. The last 2 chapters address the use of computers, including hand-held, in clinical practice—how they are currently improving care and how they may be integrated into future patient care. A glossary briefly defines more than 65 EBM terms, some of which were not discussed in the text.

This book's strengths are its clear writing and persistent emphasis on practical application of the concepts of EBM. The examples given are current and relevant, although the information on computer technology will undoubtedly be time-sensitive. It will be most useful to those who have had some background knowledge in clinical epidemiology and can use the glossary to refresh concepts or the worksheets to quickly evaluate a paper. It may also be useful to those who are seeking a very brief introduction to EBM. Ample references are given for more in-depth reading, for those who need further explanation. Its inclusion of cost-effectiveness studies and clinical practice guidelines is an advantage over other EBM texts.

REFERENCES

1. Oxman A, Sackett D, Guyatt G. Users' guides to the medical literature. I: How to get started. The Evidence-Based Medicine Working Group. JAMA 1993;270(17): 2093–2095.

Patricia A Thomas MD
Division of General
Internal Medicine
Johns Hopkins University
School of Medicine
Baltimore, Maryland

Where's the Evidence: Debates in Modern Medicine. William A Silverman. Foreword by David L Sackett. New York: Oxford University Press. 1999. Soft cover, 259 pages, $32.50

William Silverman chose the mantra of the evidence-based medicine movement as the title for his collection of previously published essays, though the subtitle is a better indicator of the contents. Silverman, a retired professor of pediatrics from Columbia University, wrote the essays for the journal *Paediatric and Perinatal Epidemiology* over the 10-year span from 1987 to 1997 and presents them here appended with published responses from readers and his own more recent observations. The essays originally ran under the title "Fumes from the Spleen" and were signed with the pseudonym "Malcontent," yet, to the author's great credit, the essays read as thoughtful commentaries rather than simple rants. The author was given free reign over the subject matter and used that freedom to address a wide variety of topics. Although Silverman has his own idea regarding recurring themes in his essays, I would identify the 2 main areas of focus as evidence and ethics. And an interesting subtext of many essays is the author's view of how these 2 areas intersect.

Dr Silverman is an unabashed proponent, even cheerleader, for the evidence-based medicine (EBM) movement. Throughout this book he pays homage to the leaders of EBM: Sackett (who wrote the forward for **Where's the Evidence: Debates in Modern Medicine**), Chalmers, and Cochrane. To Silverman's credit, he was an early convert and an articulate advocate for EBM, but his views in the late 1980s and early 1990s, which he sees as controversial, now read as simple EBM orthodoxy. Appeals for more evidence and more evidence-users have now been repeated so often as to be cliche. Never does the author question the notions that "evidence" is always good, that more evidence is better, that without evidence we should do nothing, and that with enough evidence medicine will be transformed.

But despite the title, the majority of essays in this book do not deal strictly with matters of clinical research and clinical epidemiology, but rather take on ethical issues. Silverman addresses a multitude of moral issues, from informed consent to distributive justice, from responsibility to medical futility. No topic, it seems, is beyond the grasp of his keen mind and sharp wit, but he pays particular attention to issues that directly impact the field of perinatology. The care of very-low-birthweight infants recurs in multiple essays, with Silverman warning repeatedly of the consequences of aggressive intervention. As a pediatrician, this area of medical, moral, and at times political controversy is very familiar to Silverman and serves as an example of what is wrong with modern medicine. And in addressing this problem and other ethical dilemmas, Silverman's true faith in evidence becomes clear. He believes that more evidence, more epidemiologic data, will not only lead to the better practice of medicine, but will also resolve longstanding and arguably intractable moral debates. Even the troublesome problem of whether we should be providing expensive, life-sustaining care to premature infants, who suffer a high mortality rate and an even higher likelihood of longstanding medical and developmental problems, will be resolved by better clinical and sociologic research. Ethics problems, according to Silverman, are simply clinical problems, and the resolution of both depends only on the provision of better empirical evidence. Such a notion, though philosophically suspect, is not unusual in EBM true-believers, who see values as just another attribute to be measured, quantified, and incorporated into an EBM-driven calculus. But while empirical evidence can inform ethical debates, evidence cannot resolve them; the hardest questions in medicine, including whether to resuscitate a marginal newborn, will never be answered by an appeal to a clinical trial.

Silverman's use of examples from pediatrics is understandable (he is a pediatrician

writing for an audience of pediatricians) but does limit the appeal of the essays somewhat. Although most of the topics he takes on are of interest to practitioners in other areas of medicine, some pediatric problems do not generalize well. In particular, Silverman's recurrent critique of the "never say die" attitude prevalent in the neonatal intensive care unit does not reflect the substantial changes in adult critical care. Once accused of having the same lack of interest in quality of life and distributive justice issues, adult intensivists have largely embraced the notion of limiting care based on poor prognosis, either for survival or quality of life. Pediatricians like to remind internists that children are not just little adults, but neither are their problems miniature versions of those facing grown-ups. For those involved in the care of children, the essays are likely to hit home. For those who never care for kids, making the leap from Silverman's examples takes a bit more effort.

The structure of the book is not ideal. Silverman's essays are presented in chronological order, rather than being organized by subject matter. This allows the reader to appreciate the historical evolution of the author's thoughts and the focus of the EBM movement, starting with appeals to refrain from actions without evidentiary support and progressing to more sophisticated discussions, such as how to interpret statistical presentations of data. But the chronological presentation has the reader jumping between short discussions of unconnected topics. Each essay stands alone, rendering the book more interesting when it is read in 5-minute increments, an essay at a time.

More irritating for the academic-minded reader is the way citations are dealt with. Rather than finding the references at the end of each essay, a reader interested in examining Silverman's sources must find a citation by author and year in an appendix and then find the full citation in a separate bibliography. As Silverman quotes a wide variety of medical and nonmedical writers and cites a great deal of research and research-related writing, the inquisitive reader spends a lot of time flipping through the back pages.

Despite these limitations, **Where's the Evidence** provides a chance to read the well-articulated thoughts of a well- and widely-read physician who, despite his own devotion to empirical evidence, clearly embodies those nonevidentiary traits that make for a superb clinician. Silverman's understanding of the history of medicine, his use of anecdotes (usually anathema to EBMers), and the ubiquitous literary references make these essays a pleasure to read. Although he sees himself as a bit of an academic curmudgeon, his tone is positive even when he is suffering fools and constructive even when pointing out the errors of others. Although I do not share his view of empirical evidence as a panacea for the ills of modern medicine, one cannot help but admire Silverman's intellect and reasoning skills. His essays are thought-provoking, even when no longer controversial, and his enthusiasm for improving on clinical medicine is infectious. In short, each essay is a good read, and an educational one at that. This is one book where the parts are greater than the whole.

Mark R Tonelli MD MA
Department of Medicine
and
Department of Medical History and Ethics
University of Washington
Seattle, Washington

Outcome of the Critically Ill: Medicine, Surgery and Trauma. Rade B Vukmir MD JD. New York: The Parthenon Publishing Group. 2001. Soft-cover, 188 pages, $44.

Outcome of the Critically Ill: Medicine, Surgery and Trauma offers an exhaustive review of scientific literature that describes how a variety of patients fare following admission to an intensive care unit (ICU). The text is divided into 3 "templates," one each for medicine and anesthesia/surgical ICUs and the third devoted to evaluating the effects of traumatic injury on patients. The goal of the text seems not to be how best to triage limited resources, but to allow caregivers some ability to anticipate what these patients can expect during and following their ICU stays, and to predict areas of possibly futile care. The author indicates his intended audience to include medical students and attending intensivists, as well as those practitioners who care for critically ill patients infrequently. Though informative to all, I believe the groups most likely to benefit from this book are those who have direct interactions and discussions with both critically ill patients and their families.

The "template" design is well thought out and organized. Medical, surgical, and trauma ICUs have different populations with diverse presentations, co-morbidities, and pre-existing medical conditions. Though it may be uncommon to routinely see a trauma patient with an extensive medical history, such patients would be the exception to the rule in most other units. In addition, the diagnosis may be somewhat more straightforward in the traumatically injured or post-operative patient than in the typical medical ICU admission, carrying a similar ability to better anticipate subsequent problems where the diagnosis is more secure. Owing to those differences, Dr Vukmir has smartly given each group its own dedicated section, with minimal overlap of disciplines.

The first and longest template begins with descriptions of the development and focus of the earliest ICUs. Dr Vukmir provides a brief but informative history of the first medical ICUs as places where care could be delivered to the "critically but not hopelessly ill." Following that introduction, the author subdivides the section to individually address organ systems and disease states related to those systems. Unfortunately, I found this section tedious to read, largely because of the very extensive use of percentages to describe outcomes. Though this clearly is the topic to be covered, the percentage was used so frequently that it became difficult to follow the author's intended point. These descriptions also, too frequently, did not have a reference to the date of the study in the body of the text. The other sections did not suffer from this, however, and all of the author's references are very well documented at the conclusion of each chapter. This chapter contained the only typographical error I found: on Page 15 "isotropic agent" should be "inotropic agent."

The only other criticism I have of the book involves the age of the references, none being younger than 1996. Given the plethora of reference sources cited, though, this is not a major detriment. The overall coverage of medical ICU admission diagnoses is quite thorough and provides the practitioner a good feel for expected patient outcomes as well as potential management strategies to improve those outcomes. Additionally, it gives time to nutritional deficiencies (a topic often under-appreciated in ICUs) as well as the positive impact of nursing intervention.

Anesthesia and surgical ICUs are the focus of template 2. This section is introduced with some background on the improvements in morbidity and mortality from anesthesia and surgical interventions over the last half of the 20th century, with emphasis on the impact of the institution of a dedicated unit to care for critically ill patients. This equally thorough treatise is also subdivided into or-

gan systems and includes data on some prophylactic measures to improve outcomes as well as the positive role for aggressive and early physical therapy.

The high point of this chapter is the author's extensive descriptions of the various prognostic models available. This information allows the reader additional insight into just what these percentages mean and where they derive from. He addresses models that evaluate not only mortality and morbidity but quality of life. It is this last piece of information that is far too often not conveyed effectively to patient's families when discussing the most severely injured or sick patient. Again, though somewhat dated, the source material referenced is very extensive.

The final template is devoted to a subset of surgical and medical patients, namely physical trauma patients. This section begins by discussing various mechanisms that improve survival to hospital as well as describing the nomenclature of how institutions are designated a "trauma level" status. Dr Vukmir continues with a general discussion of certain patient and mechanism-of-injury characteristics that serve as prognostic indicators of outcome. He then returns to the basic format of a systems approach to evaluating outcomes.

This section includes a more in-depth look at neurologic injury, whether it be closed head injury, spinal cord trauma, or orthopedic injury that compromises the central nervous system. As in the previous template, the author includes a very expert explanation of various outcome models. It concludes with a section on outcomes related to rehabilitation potential after a traumatic injury.

This paperback book is fairly priced at $44 and is relatively easy to read. The information it provides should prove most valuable to those who encounter these situations on an infrequent basis, but it would serve as good background resource material for those who encounter these conditions on a routine basis as well. The shining features include the exhaustive literature referenced and the complete descriptions of many of the predictive modeling systems in use today.

C Mark Bazzell MD
Department of Anesthesiology
Division of Critical Care Medicine
Mayo Clinic,
Rochester, Minnesota

Informatics for Healthcare Professionals. Kathleen M Young MA RNC. Philadelphia: FA Davis. 2000. Soft cover, illustrated, 282 pages, $29.95.

Informatics for Healthcare Professionals presents itself as a "mid-level, generic informatics book" to be used in a health care curriculum. It introduces the surprising breadth of informatics in a very readable format. Along the way it covers types of information, computer literacy, taxonomy, security, electronic systems design, and telehealth, to mention just a few.

Health care depends on information. Massive amounts of data can be created about a single patient. Those data must be considered in context to become information. Information is then assimilated into a knowledge base that can be used for medical decision-making. The first part of the book gives several examples of this process.

Wisely, the author avoids getting bogged down with introductory level discussions, such as describing word processors or spreadsheets. She also does not give any details about commercial health care information systems, even during a lengthy chapter on electronic records. This is commendable, since the concepts of record management are more important to understand than how to enter test results in any given database.

An early chapter presents the 5 "rights" of information: the right *information* available to the right *person* at the right *time* in the right *place* and in the right *amount*. These rights make up the field of health care informatics, which consists not only of health care but also computer, information, and cognitive sciences. Having the right information is also a prerequisite for evidence-based medicine. Evidence-based medicine is subsequently made easy to understand, along with the potential barriers to its implementation.

Human factors engineers address the presentation of information and potential problems. They describe well-known problems relating to bad design, such as the failure at Three-Mile Island. A list of features discusses how to avoid problems in designing human-machine interfaces. Usability is dependent on ease of learning, assistance in task performance, and error avoidance. This requires not only assessing the task, but also the expected user. An uncited source on Page 67 tells of "numerous injuries, deaths, and 'near misses' with ventilators" because of poor tube and connector design.

Classification of information is discussed in the next chapter. It shows the need for standardized and discipline-differentiated medical languages. Several examples are given of attempts to create a unified nursing language from several existing classification systems.

The chapter on electronic health records shows both their value and current shortcomings. Paper charts have been around for generations and provide a level of comfort for most practitioners; they are easily portable and can accommodate many types of data. On the other hand, they are usually limited to a single user at a time, can be lost, require physical storage facilities, and have no internal mechanism for accuracy. It would be nice to think that electronic records relieve all of these problems, but they don't. In fact they add a few of their own, most notable of which is the initial startup cost. Availability of the record in multiple locations at the same time points out the need for security. The discussion of rights and ownership of the data continues in following chapters.

One of the most useful sections of the book discusses change control, specifically in relation to automating medical information. This information could easily be used in any management course. Recognizing that there is always resistance to change, the chapter tells how to find different groups of employees and use each for their strengths. Change should be a circular process that starts with analysis; moves through design, development, and implementation; and then returns to the beginning of the cycle with analysis.

The most critical point of the book is in the chapter on information management. A section titled "Invisibility of Allied Health Professions in Data Collection" states:

> If allied health professionals are to influence the delivery of health care in managed-care environments, an information infrastructure similar to those used by the power structures that design and control the delivery and purchasing of health care in the United States must be developed.

It points out that all of the current codification systems—such as the International Classification of Diseases, the Diagnosis Related Groups, and the Physicians' Current

Procedural Terminology—ignore the practice, interventions, and outcomes attributable to allied health professionals. For example, in order for the value of respiratory care to be recognized, information has to be made available in a standardized language. A later chapter discusses how to transform information into knowledge and to use management techniques such as total quality management and continuous quality improvement.

The chapter on electronic communications tries to cover the World Wide Web, e-mail, list servers, chat rooms, firewalls, personal digital assistants, and voice recognition in about 20 pages. Most of the information is there, but in a somewhat jumbled format. For people who look for technical errors, an Internet protocol (IP) address example on Page 193 is wrong. The chapter provides good information on evaluating Web sites. With more patients looking up their conditions on-line, it is necessary for practitioners to be able to help them determine the accuracy of the data.

The section on telehealth discusses the current condition of practice. Likely venues for telehealth today are rural areas, schools, prisons, and home health service. The cost of delivery can be reduced and the need for home visits can be reduced by as much as 45%. Telehealth has already brought medical care to populations that have been poorly served in the past.

Young ends the book with a paragraph relating the need for all health care education programs to become more involved in teaching informatics. Though informatics is still an elective course in many programs—if it is available at all—the future need for information management should turn this into a core teaching subject.

This book serves its stated purpose well as an informatics guidebook. Though it would be useful as a course textbook, each section also presents enough detail to make it useful as a reference book as well.

Steven B Nelson MS RRT
Overland Park, Kansas
Mayo Pulmonary Services
Rochester, Minnesota

Respiratory & Pulmonary Medicine: July 2000-June 2001: An Internet Resource Guide. Daniel R Goldenson, editor-in-chief. Joe GN Garcia MD and Charles M Wiener MD, consulting editors. Princeton, New Jersey: eMedguides.com, Inc. 2000. Soft cover, 530 pages, $24.95.

Paper or plastic? Is there a reason to use a printed volume to look for on-line resources? **Respiratory & Pulmonary Medicine: July 2000-June 2001: An Internet Resource Guide** tries to demonstrate the value of old methods over new. This book is part of a series published in conjunction with eMedguides.com and sponsored by Bristol-Myers Squibb Company. The series covers about 20 medical specialties. The unique feature of this series is that it is also available on a Web site (www.eMedguide.com) that directly reflects the organization of each book.

The book is organized into 2 parts, the first specific to respiratory and pulmonary medicine and the second for general medical topics. Each listing consists of a humanly comprehensible title, the URL (universal record locator; the "http://. . . " text string), a short descriptive paragraph, and a rating. Each site is given 1 to 3 stars, with 3 showing a great depth of information and 1 just meeting the inclusion criteria. The sites are selected by a medical research staff.

The respiratory section starts with an extensive list of reference materials, including on-line journals, recently published books, continuing education sources, and related organizations. It continues with sections on physiology, symptoms, diagnostics, procedures, and pharmacology. The largest section covers diseases and disorders, with 83 topics.

The general medicine section includes everything from pain management to office management. It is a handy reference for broad topics that are only needed occasionally.

Curiously, the page numbers in the table of contents are out of order throughout the book, but the index pages are correct.

The reader may wonder why a book is required to search the Internet. An example may help. In the disease section there are 4 references for the topic "bronchiectasis." They are well-known sites that give very good definitions of the disease, along with symptoms, radiology findings, and other supporting data. A search for the same term on popular Web search engines gave the following numbers of references: Altavista 19,620; Google 13,300; Lycos 8,773; WebCrawler 300; WebMD 25; Yahoo 5,440.

It is quickly obvious that there are too many choices. The book may not provide the "best" reference, if one could even be determined, but it does give a manageable number of reasonably good resources.

A related question that comes to mind is, "Why try to capture something that changes so quickly?" The data in a book may well be over a year old by the time it is finally printed. Web sites can appear and disappear in a matter of months and change completely in the interim. The indexers of this book included sites that would have some longevity, but even so, comparing the print version to the on-line version shows the effect of the recent "dot.com" disasters. Section 11.1, "Abstract, Citation, and Full-Text Search Tools," lists 4 items. In August 2001 only one of the sites was still reachable. By contrast, the on-line section on neuromuscular diseases has added 5 resources and corrected a bad Internet address.

The value of the printed versus on-line version can still be debated. The only reason the book is actually required is to obtain the access code printed on the inside cover. Without that, much of the on-line version is not accessible. However, the Web site offers a suggestion: contact a pharmaceutical representative for a complimentary copy for qualified medical professionals. The on-line version appears to be updated regularly, providing the benefit that should be expected.

Though the paper version provides a comfort factor for the technologically-challenged and also provides a set of very good references, the on-line version still wins, in my opinion, with the ability to be updated as better references are found. Plastic, please.

Steven B Nelson MS RRT
Overland Park, Kansas
Mayo Pulmonary Services
Rochester, Minnesota

Appreciation of Reviewers

The Editors of RESPIRATORY CARE are deeply grateful to the following persons who have contributed their expertise and time to the reviewing of manuscripts and OPEN FORUM abstracts during the past year.

Russell A Acevedo MD
Alexander B Adams MPH RRT FAARC
Moira L Aitken MD
Richard K Albert MD
Kathryn L Anderson PhD RN
Jose A L Arruda MD
Jeanette Asselin MS RRT
David Au MD
Michael L Ault MD
Michael J Banner PhD RRT
Steven J Barker MD
Thomas A Barnes EdD RRT FAARC
Sherry L Barnhart RRT
Peter W Bates MD
Joshua O Benditt MD
Peter Betit RRT FAARC
Akhil Bidani MD PhD
Howard J Birenbaum MD
Michael J Bishop MD
Craig Patrick Black PhD RRT
Griffith M Blackmon MD MPH
Lluis L Blanch MD PhD
Paul B Blanch RRT
Susan B Blonshine RPFT RRT FAARC
Louis J Boitano RRT
Richard D Branson RRT FAARC
Charlie G Brooks Jr MEd RRT FAARC
Lee J Brooks MD
Naoto Burioka MD
David M Burns MD
Suzanne M Burns RN MSN RRT
Carlos A Camargo Jr MD DrPH
Margaret L Campbell RN MSN CS
Robert S Campbell RRT FAARC
Sammy C Campbell MD
Waldemar A Carlo MD
Steven Cattapan MD
Bartolome R Celli MD
David W Chang EdD RRT
Robert L Chatburn RRT FAARC
Ira M Cheifetz MD
Jean Daniel Chiche MD
Kent L Christopher MD RRT
Cynthia H Cole MD MPH
Thomas C Corbridge MD
Paul M Cox Jr MD
Gerard J Criner MD
Bruce H Culver MD
Joseph R Custer MD
Michael P Czervinske RRT
David H Dail MD
Robert L Danner MD
Timothy A Davidson MD
Kathleen Deakins RRT
Steven A Deem MD
Bob R Demers RRT
Vijay M Deshpande MS RRT FAARC
Rajiv Dhand MD
Thomas A Dillard MD
Myrna B Dolovich P Eng
Claudio F Donner MD
Patricia Ann Doorley MS RRT
Sara L Douglas PhD CRNP
John B Downs MD
Didier D Dreyfuss MD
Charles G Durbin Jr MD FAARC
E Wesley Ely Jr MD MPH
Paul L Enright MD
Lawrence J Epstein MD
Mark L Everard MB ChB MD
Daniel J Farrell MEd RRT CPFT
James B Fink MS RRT FAARC
Eugene C Fletcher MD
Robert R Fluck Jr MS RRT
Richard M Ford RRT
Catherine Foss RRT
Mitchell Friedman MD
Ronald B George MD
Audrey G Gift PhD RN
Robert Chapman Gilkeson Jr MD
Reda Girgis MD
Rodolfo I Godinez MD PhD
Christopher H Goss MD MSc
John M Graybeal CRT
George W Gross MD
Loic Guillevin MD
Jesse B Hall MD
Teal S Hallstrand MD MPH
John Hannigan MBA RRT
Ken Hargett RRT
Umur S Hatipoglu MD
Zvi J Herschman MD
Dean R Hess PhD RRT FAARC
Mark J Heulitt MD FAARC
Nicholas S Hill MD
Lana Hilling CRT
Robert Hirnle MS RRT
Ronald B Hirschl MD
Leslie A Hoffman PhD RN
Shirley J Holt RRT
John M Hughes MEd RRT
Hideaki Imanaka MD
Dennis Irlbeck
Charles G Irvin PhD
Michael A Jantz MD
Robert M Kacmarek PhD RRT FAARC
Richard H Kallet MS RRT
Thomas J Kallstrom RRT FAARC
Vishesh Kapur MD
Anna-Luise A Katzenstein MD
Lucy Kester RRT MBA FAARC
Max Kirmse MD
Marin H Kollef MD
David H Kupferberg MD
James P Lamberti MD
Esther L Langmack MD

Chae Man Lim MD
Neil R MacIntyre MD FAARC
Nicholas J Macmillan RRT
James Maguire PhD RRT
Barry Make MD
Harold L Manning MD
Constantine A Manthous MD
Gregory P Marelich MD
John J Marini MD
Rex Alan Marley MS CRNA RRT
Paul J Mathews PhD RRT
Andrew W McKibben MD
Benjamin D Medoff MD
Paula M Meek PhD RN
Rachel L Miller MD
Omar A Minai MD
Pamela L Minkley CPFT RRT RPSGT
Shelley C Mishoe PhD RRT FAARC
Carl D Mottram RRT RPFT
Simon J Newell MD
Jon O Nilsestuen PhD RRT FAARC
Masaji Nishimura MD
Timothy B Op't Holt EdD RRT
James R Patterson MD
Marcy F Petrini PhD
Robert Pettignano MD
Alan L Plummer MD
Jenni L Raake RRT
Joseph L Rau PhD RRT FAARC
Sue A Ravenscraft MD
Gregory J Redding MD
Jean-Damien Ricard MD
Jesse D Roberts MD
Gustavo J Rodrigo MD
Marc S Rovner MD
Brian H Rowe MD MSc
Gordon D Rubenfeld MD MSc
Bruce K Rubin MD
Gregg L Ruppel MEd RRT RPFT FAARC
Katie Sabato MS RRT
John S Sabo MS RRT
John W Salyer RRT FAARC
Allan B Saposnick MS RRT
Catherine S H Sassoon MD
Gregory A Schmidt MD
Theresa Ryan Schultz RRT RN
Paul A Selecky MD
Sam R Sharar MD
David C Shelledy PhD RRT
Vandy Sherbin MD
John W Shigeoka MD
Kevin L Shrake MA RRT FAARC
Gerard A Silvestri MD MS
Michael W Sipes RRT
Dorsett D Smith MD
Helen M Sorenson MA RRT
Greg Spratt RRT CPFT
Robert St John MSN RN RRT
John L Stauffer MD
Karen J Stewart RRT
James K Stoller MS MD
Robert Suh MD
Warren R Summer MD
Rozanna Templin CCPT
John E Thompson RRT
Martin J Tobin MD
G Iain Town MBBS
Narendra S Trivedi MD
Teresa A Volsko RRT
Bennet M Wang MD
Jack Wanger MS RRT RPFT
Jeffrey J Ward MEd RRT
Michael E Wechsler MD
Barbara G Wilson MEd RRT
Dennis R Wissing PhD RRT
Phunsup Wongsurakiat MD
Jan Zielinski MD
Richard L ZuWallack MD

RESPIRATORY CARE OPEN FORUM 2002

RESPIRATORY CARE welcomes abstracts of scientific reports on any aspect of respiratory care presented as

- an original study
- the evaluation of a method, device, or protocol
- a case or case series

If your abstract is accepted for publication in RESPIRATORY CARE, you will be invited to present it at the 48th International Respiratory Congress in Tampa, Florida.

See the **Call for Abstracts 2002** in this issue for more information.

Deadline for Submissions is April 30, 2002

Author Index to Volume 46 (2001)

A

Adams AB: Catheters for tracheal gas insufflation, **46(2):177** *conference proceedings*

Adams AB, *coauthor:* Han JN, **46(9):891**

Adams AB et al: Static and dynamic pressure-volume curves reflect different aspects of respiratory system mechanics in experimental acute respiratory distress syndrome, **46(7):686** *research article*

Adrogué HE & Adrogué HJ: Acid-base physiology, **46(4):328** *review*

Adrogué JH, *coauthor:* Adrogué HE, **46(4):328**

Ahmed A, *coauthor:* Muhammad AA, **46(7):702**

Alonso JA, *coauthor:* Kallet RH, **46(1):49**

Ambrosino N: Advances in cardiopulmonary rehabilitation, **46(8):834** *books, films, tapes, & software*

Anderson J: Basic mathematics for the health-related professions, **46(10):1059** *books, films, tapes, & software*

Arruda JAL, *coauthor:* Sassoon CSH, **46(4):327**

Axton KL Jr: Pulmonary physiology, 5th ed, **46(7):721** *books, films, tapes, & software*

Ayers LW, *coauthor:* Cordero L, **46(8):783**

B

Balasubramaniam V & Wagener JS: Kendig's disorders of the respiratory tract in children, 6th ed, **46(1):68** *books, films, tapes, & software*

Barnes TA: Mosby's diagnostic and laboratory test reference, 4th ed, **46(2):200** *books, films, tapes, & software*

Barnes TA: Tracheal intubation: training and retention, **46(3):227** *editorial*

Barrington KJ: Chronic lung disease in early infancy, **46(8):829** *books, films, tapes, & software*

Barry HC: Users' guide to the medical literature: a manual for evidence-based clinical practice, **46(12):1450** *books, films, tapes, & software*

Barry HC: Users' guide to the medical literature: essentials of evidence-based clinical practice **46(12):1450**, *books, films, tapes, & software*

Bates PW: Comprehensive respiratory medicine, **46(3):279** *books, films, tapes, & software*

Baum GL: Interstitial lung disease, 3rd ed, **46(4):408** *books, films, tapes, & software*

Bazzell CM: Outcome of the critically ill: medicine, surgery and trauma, **46(12):1454** *books, films, tapes, & software*

Beckett RG: Pulmonary rehabilitation: guidelines to success, 3rd ed, **46(8):833** *books, films, tapes, & software*

Bishop MJ: Unintended consequences of artificial airways: replacement parts are never as good as the factory-installed, **46(10):1010** *editorial*

Bishop MJ et al: Recertification of respiratory therapists' intubation skills one year after initial training: an analysis of skill retention and retraining, **46(3):234** *research article*

Blanch LL: Clinical studies of tracheal gas insufflation, **46(2):158** *conference proceedings*

Blanch PB: An evaluation of ventilator reliability: a multivariate, failure time analysis of 5 common ventilator brands, **46(8):789** *research article*

Borges GS, *coauthor:* Santos JWA, **46(1):53**

Branson RD: Dual control modes, closed loop ventilation, handguns, and tequila, **46(3):232** *editorial*

Broach SD & Durbin CG Jr: A randomized, controlled, clinical trial of a chemically-reactive heated humidifier, **46(1):37** *research article*

Buist AS, *coauthor:* Pauwels RA, **46(8):798**

Bunnell JB: High-frequency jet ventilation, **46(8):826** *letter*

Burns DM, *coauthor:* Mitsuoka M, **46(9):902**

C

Çakar N, *coauthor:* Adams AB, **46(7):686**
Calverley PMA, *coauthor:* Pauwels RA, **46(8):798**
Camargo CA, *coauthor:* Rowe BH, **46(12):1380**
Campbell AR, *coauthor:* Siobal M, **46(10):1012**
Canfield J, *coauthor:* Shafazand S, **46(6):595**
Cantwell GP, *coauthor:* Kuluz JW, **46(9):897**
Cardell J: Pocket companion for critical care nursing, **46(2):202** *books, films, tapes, & software*
Chang DW: Clinical practice in respiratory care, **46(3):282** *books, films, tapes, & software*
Chatburn RL: Device evaluation: a critique, **46(3):273** *letter*
Chatburn RL: Introduction to research in the health sciences, 4th ed, **46(11):1307** *books, films, tapes, & software*
Chatburn RL: Outcomes research in respiratory care, **46(11):1215** *conference proceedings*
Chatburn RL, *coauthor:* Freed ML, **46(5):466**
Chatburn RL & Primiano FP Jr: A new system for understanding modes of mechanical ventilation, **46(6):604** *special article*
Chatburn RL & Primiano FP Jr: Decision analysis for large capital purchases: how to buy a ventilator, **46(10):1038** *special article*
Chatmongkolchart S et al: Evaluation of inspiratory rise time and inspiration termination criteria in new-generation mechanical ventilators: a lung model study, **46(7):666** *research article*
Chatmongkolchart S et al: Heliox delivery with noninvasive positive pressure ventilation: a laboratory study, **46(3):248** *research article*
Chen XJ, *coauthor:* Han JN, **46(9):891**
Chiu CY, *coauthor:* Hoberty PD, **46(7):694**
Christian M, *coauthor:* Freed ML, **46(5):466**
Christopher KL et al: Preliminary observations of transtracheal augmented ventilation for chronic severe respiratory disease, **46(1):15** *research article*
Chuang KH, *coauthor:* Doyle DM, **46(11):1258**
Cohn HE, *coauthor:* Nordstrom CR, **46(6):601**
Cook DJ, *coauthor:* Meade MO, **46(12):1408**
Cordero L et al: A comparison of two airway suctioning frequencies in mechanically ventilated, very-low-birth-weight infants, **46(8):783** *research article*
Corral W, *coauthor:* Kallet RH, **46(10):1024**
Cowan T et al: Effect of inner cannula removal on the work of breathing imposed by tracheostomy tubes: a bench study, **46(5):460** *research article*
Currie D, *coauthor:* Peruzzi WT, **46(3):243**

D

Dahm C: Fraser and Paré's diagnosis of diseases of the chest, 4th ed, **46(3):278** *books, films, tapes, & software*
Dalton HJ: Handbook of pediatric intensive care, 3rd ed, **46(5):492** *books, films, tapes, & software*
Dank JP: Skin signs of systemic disease, 3rd ed, **46(4):409** *books, films, tapes, & software*
Dauterive R, *coauthor:* Doyle DM, **46(11):1258**
Dawn SK et al: Multidetector-row spiral computed tomography in the diagnosis of thoracic diseases, **46(9):912** *review*
Delgado E et al: Effects of continuous, expiratory, reverse, and bi-directional tracheal gas insufflation in conjunction with a flow relief valve on delivered tidal volume, total positive end-expiratory pressure, and carbon dioxide elimination: a bench study, **46(6):577** *research article*
Delgado E et al: Monitoring and humidification during tracheal gas insufflation, **46(2):185** *conference proceedings*
Demers B: The multiskilled respiratory therapist: a competency-based approach, **46(10):1057** *books, films, tapes, & software*
DePriest JL: Weaning parameters: who cares!, **46(9):946** *letter*
Dhillon RS, *coauthor:* Muhammad AA, **46(7):702**
Diehl SS, *coauthor:* Christopher KL, **46(1):15**
Dixon AE: Lecture notes on respiratory medicine, 5th ed, **46(1):68** *books, films, tapes, & software*
Doyle DM et al: Translating evidence into practice: pursuing perfection in pneumococcal vaccination in a rural community, **46(11):1258** *conference proceedings*
Dreyfuss D, *coauthor:* Ricard J-D, **46(9):888**
Dubinsky T, *coauthor:* Krejci CS, **46(9):932**
Durbin CG Jr: Radial arterial lines and sticks: what are the risks?, **46(3):229** *editorial*
Durbin CG Jr, *coauthor:* Broach SD, **46(1):37**
Durbin CG Jr, *coauthor:* Littlewood K, **46(12):1392**
Durning SM, *coauthor:* Schultz TR, **46(8):772**
Dyer RA, *coauthor:* Foland JA, **46(10):1019**

E

Edmonds ML: Evidence-based medicine: how to practice and teach EBM, 2nd ed, **46(11):1306** *books, films, tapes, & software*
Edmonds ML, *coauthor:* Rowe BH, **46(12):1380**
El-Khatib MF & Jamaleddine G: Mean alveolar pressure during constant-flow and constant-pressure inflation of diseased lungs, **46(7):678** *research article*
Ellrodt AG, *coauthor:* Doyle DM, **46(11):1258**
Epstein SK & Singh N: Respiratory acidosis, **46(4):366** *review*
Erwin PJ: MD consult, **46(4):411** *RC web sites*

F

Farber HJ & Langham B: Evidence-based asthma management, **46(11):1307** *books, films, tapes, & software*

Farber JL, *coauthor:* Nordstrom CR, **46(6):601**

Ferranti RD & Votto JJ: Voices and choices: young people who use assisted ventilation: their health and social care, and education *and* Voices and choices: young people who use assisted ventilation: bibliography and analysis of the literature, **46(8):830** *books, films, tapes, & software*

Fields J: Entry level respiratory therapist exam guide, 3rd ed, **46(10):1057** *books, films, tapes, & software*

Finch D: Textbook of respiratory medicine, 3rd ed, **46(3):280** *books, films, tapes, & software*

Flemons WW, *coauthor:* Heitman SJ, **46(12):1418**

Fluck RR Jr: Principles of physiology, 3rd ed, **46(7):719** *books, films, tapes, & software*

Foland JA et al: Airway pressure release ventilation with a short release time in a child with acute respiratory distress syndrome, **46(10):1019** *case report*

Foss CM: All you really need to know to interpret arterial blood gases, 2nd ed, **46(1):71** *books, films, tapes, & software*

Foster GT et al: Respiratory alkalosis, **46(4):384** *review*

Francis B, *coauthor:* Schultz TR, **46(8):772**

Freed L, *coauthor:* Freed ML, **46(5):466**

Freed ML et al: Electrical stimulation for swallowing disorders caused by stroke, **46(5):466** *research article*

G

Gegenheimer C, *coauthor:* Cowan T, **46(5):460**

Gelman B, *coauthor:* Kuluz JW, **46(9):897**

Giacoppe GN: Procedures and techniques in intensive care medicine, 2nd ed, **46(5):491** *books, films, tapes, & software*

Giacoppe GN: Textbook of critical care, 4th ed, **46(3):281** *books, films, tapes, & software*

Gibbons WJ, *coauthor:* Muhammad AA, **46(7):702**

Gillette MA, *coauthor:* Hess DR, **46(2):119**

Gillette MA & Hess DR: Ventilator-induced lung injury and the evolution of lung-protective strategies in acute respiratory distress syndrome, **46(2):130** *conference proceedings*

Godinez RI, *coauthor:* Schultz TR, **46(8):772**

Goldberg S: A clinician's guide to tuberculosis, **46(10):1060** *books, films, tapes, & software*

Gotway MB, *coauthor:* Dawn SK, **46(9):912**

Granger WM: Cardiopulmonary anatomy and physiology, **46(10):1060** *books, films, tapes, & software*

Guyatt GH, *coauthor:* Meade MO, **46(12):1408**

Guyatt GH, *coauthor:* Montori VM, **46(11):1201**

H

Hales R, *coauthor:* Schultz TR, **46(8):772**

Hampson NB: Hyperbaric medicine practice, 2nd ed, **46(4):405** *books, films, tapes, & software*

Han JN et al: Effects of decreasing the frequency of ventilator circuit changes to every 7 days on the rate of ventilator-associated pneumonia in a Beijing hospital, **46(9):891** *research article*

Haynes JM: Lung collapse during low tidal volume ventilation in acute respiratory distress syndrome, **46(5):489** *letter*

Heitman SJ & Flemons WW: Evidence-based medicine and sleep apnea, **46(12):1418** *conference proceedings*

Herridge MS, *coauthor:* Meade MO, **46(12):1368**

Hess DR: response to Bunnell, **46(8):827** *letter*

Hess DR: The evidence for secretion clearance techniques, **46(11):1276** *conference proceedings*

Hess DR: Tracheal gas insufflation: overcoming obstacles to clinical implementation, **46(2):198** *conference summary*

Hess DR, *coauthor:* Chatmongkolchart S, **46(3):248, 46(7):666**

Hess DR, *coauthor:* Gillette MA, **46(2):130**

Hes DR, *coauthor:* MacIntyre NR, **46(2):118**

Hess DR, *coauthor:* Mishoe SC, **46(11):1200**

Hess DR & Gillette MA: Tracheal gas insufflation and related techniques to introduce gas flow into the trachea, **46(2):119** *conference proceedings*

Hete B, *coauthor:* Delgado E, **46(6):577**

Heulitt MJ, *coauthor:* Holt SJ, **46(1):26**

Hirnle RW: Pharmacology for health professionals, **46(9):952** *books, films, tapes, & software*

Hoberty PD et al: Staffing exercise sessions in pulmonary rehabilitation, **46(7):694** *research article*

Hoberty RJ, *coauthor:* Hoberty PD, **46(7):694**

Hoffman LA, *coauthor:* Delgado E, **46(2):185, 46(6):577**

Holt SJ et al: An evaluation of Automode, a computer-controlled ventilator mode, with the Siemens Servo 300A ventilator, using a porcine model, **46(1):26** *research article*

Hopper KB: Medicine meets virtual reality 2000. Envisioning healing: interactive technology and the patient-practitioner dialogue, **46(11):1309** *books, films, tapes, & software*

Hurd SS, *coauthor:* Pauwels RA, **46(8):798**

Hussey JD, *coauthor:* Bishop MJ, **46(3):234**

I

Irvin CG: Lung function tests: physiological principles and clinical applications, **46(1):70** *books, films, tapes, & software*

Ito Y, *coauthor:* Nishiyama O, **46(7):698**
Izenberg S, *coauthor:* Cowan T, **46(5):460**

J

Jacobson AF, *coauthor:* Lewis DH, **46(9):940**
Jacobson KL, *coauthor:* Mitsuoka M, **46(9):902**
Jamaleddine G, *coauthor:* El-Khatib MF, **46(7):678**
Jantz MA: Acute exacerbation of idiopathic pulmonary fibrosis and fibroproliferative acute respiratory disease syndrome: similar disease, similar treatment? **46(7):664** *editorial*
Jenkins CR, *coauthor:* Pauwels RA, **46(8):798**
Jirapaet K-S et al: Comparison of high-frequency flow interruption ventilation and hyperventilation in persistent pulmonary hypertension of the newborn, **46(6):586** *research article*
Johnson FW, *coauthor:* Mitsuoka M, **46(9):902**
Johnson NT: Principles and practice of sleep medicine, 3rd ed, **46(6):625** *books, films, tapes, & software*
Johnson RL: Allergic diseases: diagnosis and treatment, 2nd ed, **46(6):624** *books, films, tapes, & software*
Jonson E, *coauthor:* Siobal M, **46(10):1012**
Jorgenson SJ, *coauthor:* Christopher KL, **46(1):15**

K

Kacmarek RM: Complications of tracheal gas insufflation, **46(2):167** *conference proceedings*
Kacmarek RM, *coauthor:* Chatmongkolchart S, **46(3):248, 46(7):666**
Kallet RH: Response to Haynes, **46(5):489** *letter*
Kallet RH, *coauthor:* Siobal M, **46(10):1012**
Kallet RH et al: Implementation of a low tidal volume ventilation protocol for patients with acute lung injury or acute respiratory distress syndrome, **46(10):1024** *special article*
Kallet RH et al: Lung collapse during low tidal volume ventilation in acute respiratory distress syndrome, **46(1):49** *case report*
Kane GC, *coauthor:* Nordstrom CR, **46(6):601**
Karmy-Jones R: A dream of the heart: the life of John H Gibbon Jr, father of the heart-lung machine, **46(2):203** *books, films, tapes, & software*
Katz JA, *coauthor:* Kallet RH, **46(1):49**
Kester L, *coauthor:* Stoller JK, **46(3):238**
Khanna A & Kurtzman NA: Metabolic alkalosis, **46(4): 354** *review*
Kiatchuskul P, *coauthor:* Jirapaet K-S, **46(6):586**
Kinninger KH, *coauthor:* Mitsuoka M, **46(9):902**
Kirmse M: Rapid interpretation of ventilator waveforms, **46(2):201** *books, films, tapes, & software*
Kolatat T, *coauthor:* Jirapaet K-S, **46(6):586**
Kott B, *coauthor:* Lewis DH, **46(9):940**
Kraemer R, *coauthor:* Siobal M, **46(10):1012**
Kraut JA & Madias NE: Approach to patients with acid-base disorders, **46(4):392** *review*
Krejci CS et al: Thoracic sonography, **46(9):932** *review*
Kulkarni P, *coauthor:* Cowan T, **46(5):460**
Kuluz JW et al: The fraction of inspired oxygen in infants receiving oxygen via nasal cannula often exceeds safe levels, **46(9):897** *research article*
Kume H, *coauthor:* Nishiyama O, **46(7):698**
Kurtzman NA, *coauthor:* Khanna A, **46(4):354**
Kuschner WG, *coauthor:* Shafazand S, **46(6):595**

L

Lakshminarayan S, *coauthor:* Bishop MJ, **46(3):234**
Lamphere T: Pathology for the health-related professions, 2nd ed, **46(10):1058** *books, films, tapes, & software*
Landry MD & Sibbald WJ: From data to evidence: evaluative methods in evidence-based medicine, **46(11):1226** *conference proceedings*
Lands LC, *coauthor:* Seller L, **46(3):263**
Langham B, *coauthor:* Farber HJ, **46(11):1307**
Lanni HA: Allen's test: fact or myth? **46(3):274** *letter*
Lee JS: Pulmonary pathophysiology, **46(7):720** *books, films, tapes, & software*
LeGrand TS: Handbook of hemodynamic monitoring, **46(1):67** *books, films, tapes, & software*
Lemons D, *coauthor:* Siobal M, **46(10):1012**
Lewis DH et al: Single-photon emission tomography imaging of the chest, **46(9):940** *review*
Liben S, *coauthor:* Seller L, **46(3):263**
Lin RJ, *coauthor:* Schultz TR, **46(8):772**
Littlewood K & Durbin CG Jr: Evidenced-based airway management, **46(12):1392** *conference proceedings*
Liu YP, *coauthor:* Han JN, **46(9):891**
Logemann JA, *coauthor:* Peruzzi WT, **46(3):243**
Luce JM, *coauthor:* Kallet RH, **46(10):1024**
Luo DM, *coauthor:* Han JN, **46(9):891**

M

Ma S, *coauthor:* Han JN, **46(9):891**
MacIntyre NR: Chronic obstructive pulmonary disease management: the evidence base, **46(11):1294** *conference proceedings*
MacIntyre NR:Innovations in mechanical ventilation: what are (and what should be) the drivers? **46(3):267** *special article*
MacIntyre NR: Intratracheal catheters as drug delivery systems, **46(2):193** *conference proceedings*
MacIntyre NR: Tracheal gas insufflation, **46(2):118** *conference foreword*

MacIntyre NR: response to DePriest, **46(9):947** *letter*
Maclean JR, *coauthor:* Mishoe SC, **46(11):1236**
Madias NE, *coauthor:* Kraut JA, **46(4):392**
Mahon T, *coauthor:* Kuluz JW, **46(9):897**
Marchiori RC, *coauthor:* Santos JWA, **46(1):53**
Marini JJ, *coauthor:* Adams AB, **46(7):686**
Marini JJ, *coauthor:* Han JN, **46(9):891**
Marks JD, *coauthor:* Kallet RH, **46(1):49**
Marley RA: Respiratory care equipment, 2nd ed, **46(9): 951** *books, films, tapes, & software*
Marr KA: Fungal diseases of the lung, 3rd ed, **46(6):623** *books, films, tapes, & software*
Martens SK: AIDS sourcebook, 2nd ed, **46(9):952** *books, films, tapes, & software*
Martin J, *coauthor:* Foland JA, **46(10):1019**
Massey L, *coauthor:* Bishop MJ, **46(3):234**
McKone E: Principles of exercise testing and interpretation, including pathophysiology and clinical applications, 3rd ed, **46(7):721** *books, films, tapes, & software*
McLaughlin GE, *coauthor:* Kuluz JW, **46(9):897**
Meade MO & Herridge MS: An evidence-based approach to acute respiratory distress syndrome, **46(12):1368** *conference proceedings*
Meade MO et al: Weaning from mechanical ventilation: the evidence from clinical research, **46(12):1408** *conference proceedings*
Medoff BD: Irwin and Rippe's intensive care medicine, 4th ed, **46(5):491** *books, films, tapes, & software*
Mhanna MJ, *coauthor:* Foland JA, **46(10):1019**
Michalowski P, *coauthor:* Bishop MJ, **46(3):234**
Michel GT, *coauthor:* Santos JWA, **46(1):53**
Miller KG: A useful oxygen dilution formula, **46(10):1055** *letter*
Mishoe SC & Hess DR: Evidence-based medicine in respiratory care, **46(11):1200** *conference foreword*
Mishoe SC & Maclean JR: Assessment of health-related quality of life, **46(11):1236** *conference proceedings*
Mitsuoka M et al: Utility of measurements of oxygen cost of breathing in predicting success or failure in trials of reduced mechanical ventilatory support, **46(9):902** *research article*
Moen SG, *coauthor:* Peruzzi WT, **46(3):243**
Montori VM & Guyatt GH: What is evidence-based medicine and why should it be practiced?, **46(11):1201** *conference proceedings*
Morfei J: Handbook of fluid, electrolyte, and acid-base imbalances, **46(4):404** *books, films, tapes, & software*
Muhammad AA et al: Co-existing granular cell tumor and adenocarcinoma of the lung: a case report and review of the literature, **46(7):702** *case report*
Mullahoo K, *coauthor:* Seller L, **46(3):263**
Müller AA, *coauthor:* Santos JWA, **46(1):53**

N

Nahum A: Animal and lung model studies of tracheal gas insufflation, **46(2):149** *conference proceedings*
Napoli L, *coauthor:* Schultz TR, **46(8):772**
Naylor JK: Interventional pulmonology, **46(2):200** *books, films, tapes, & software*
Nelson SB: Evidence-based medicine: online resources, **46(11):1311** *RC web sites*
Nelson SB: Informatics for healthcare professionals, **46(12):1455** *books, films, tapes, & software*
Nelson SB: Respiratory & pulmonary medicine: July 2000-June 2001: an internet resource guide, **46(12):1456** *books, films, tapes, & software*
Nelson SB: Super searchers on health & medicine: the online secrets of top health & medical researchers, **46(11):1309** *books, films, tapes, & software*
Nikander K, *coauthor:* Turpeinen M, **46(1):43**
Nishiyama O et al: Effect of prolonged low-dose methylprednisolone therapy in acute exacerbation of idiopathic pulmonary fibrosis, **46(7):698** *case report*
Noblett KE: Aerosols and the profession of respiratory care: leading the way out of the fog, **46(3):275** *letter*
Nordstrom CR et al: Bronchial atresia with relapsing pulmonary infection in a middle-aged man, **46(6):601** *case report*
Novotny T, *coauthor:* Foland JA, **46(10):1019**

O

Olson CM: Decisions and evidence in medical practice: applying evidence-based medicine to clinical decision making, **46(11):1305** *books, films, tapes, & software*
Op't Holt TB: Cardiogenic triggering observed in a patient with acute respiratory distress syndrome, **46(10):1054** *letter*
Op't Holt TB, *coauthor:* Cowan T, **46(5):460**
Orens DK, *coauthor:* Stoller JK, **46(3):238**

P

Park WY: Cardiopulmonary system, **46(1):69** *books, films, tapes, & software*
Patterson JR: Chest radiology companion, **46(9):948** *books, films, tapes, & software*
Pauwels RA et al: Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: National Heart, Lung, and Blood Institute and World Health Organization Global Initiative for Chronic Obstructive Lung Disease (GOLD): executive summary, **46(8):798** *special article*
Pearl RG: The haemodynamic effects of nitric oxide, **46(5): 494** *books, films, tapes, & software*

Peruzzi WT et al: Assessment of aspiration in patients with tracheostomies: comparison of the bedside colored dye assessment with videofluoroscopic examination, **46(3):243** *research article*
Petty TL: The future of respiratory care, **46(11):1304** *letter*
Petty TL, *coauthor:* Christopher KL, **46(1):15**
Petty TL, *coauthor:* Spratt G, **46(5):475**
Pierson DJ: New international guidelines for chronic obstructive pulmonary disease, **46(8):768** *editorial*
Pierson DJ: The future of respiratory care, **46(7):705** *special article*
Pinsky MR, *coauthor:* Delgado E, **46(2):185, 46(6):577**
Powrie D: Pulmonary diseases, **46(6):622** *books, films, tapes, & software*
Primiano FP Jr, *coauthor:* Chatburn RL, **46(6):604, 46(10):1038**

R

Reyes JJ: Say it in Spanish: a guide for health care professionals, 2nd ed, **46(10):1063** *books, films, tapes, & software*
Ricard J-D & Dreyfuss D: Ventilator circuit changes: "wu wei" may save time, labor, and money, **46(9):888** *editorial*
Rowe BH et al: Evidence-based treatments for acute asthma, **46(12):1380** *conference proceedings*
Rubenfeld GD: Understanding why we agree on the evidence but disagree on the medicine, **46(12):1442** *conference summary*

S

Salazar AM, *coauthor:* Nordstrom CR, **46(6):601**
Sananes M, *coauthor:* Cordero L, **46(8):783**
Sanders RC, *coauthor:* Holt SJ, **46(1):26**
Santos JWA et al: Pneumonitis after intravenous self-administration of solvent, **46(1):53** *case report*
Sassoon CSH: Fluid, electrolyte, and acid-base physiology: a problem-based approach, 3rd ed, **46(4):404** *books, films, tapes, & software*
Sassoon CSH, *coauthor:* Foster GT, **46(4):384**
Sassoon CSH & Arruda JAL: Acid-base disturbance, **46(4):327** *review series foreword*
Schecter W, *coauthor:* Siobal M, **46(10):1012**
Schleien CL, *coauthor:* Kuluz JW, **46(9):897**
Schneider Filho A, *coauthor:* Santos JWA, **46(1):53**
Schultz TR et al: Weaning children from mechanical ventilation: a prospective randomized trial of protocol-directed *versus* physician-directed weaning, **46(8):772** *research article*
Sell S: Quick reference to critical care, **46(9):953** *books, films, tapes, & software*
Seller L et al: Weaning to extubation directly from high-frequency oscillatory ventilation in an infant with cystic lung disease and persistent air leak: a strategy for lung protection, **46(3):263** *case report*
Serrano T: The lack of data on off-label use of noninvasive positive pressure ventilation in children, **46(3):276** *letter*
Shafazand S et al: Improved quality of life among patients completing a pulmonary rehabilitation program: one center's early experience, **46(6):595** *research article*
Shapiro H, *coauthor:* Christopher KL, **46(1):15**
Shimizu M, *coauthor:* Nishiyama O, **46(7):698**
Sibbald WJ, *coauthor:* Landry MD, **46(11):1226**
Sikka P, *coauthor:* Muhammad AA, **46(7):702**
Silverman HJ, *coauthor:* Kallet RH, **46(10):1024**
Singh N, *coauthor:* Epstein SK, **46(4):366**
Siobal M: Tracheal-innominate artery fistula caused by the endotracheal tube tip: case report and investigation of a fatal complication of prolonged intubation, **46(10):1012** *case report*
Siobal MS, *coauthor:* Kallet RH, **46(1):49**
Slade JB Jr: Hyperbaric facility safety: a practical guide, **46(4):406** *books, films, tapes, & software*
Slonim AD: Studying a study and testing a test: how to read the medical evidence, 4th ed, **46(12):1451** *books, films, tapes, & software*
Sottiaux TM: Patient-ventilator interactions during volume-support ventilation: asynchrony and tidal volume instability—a report of three cases, **46(3):255** *case report*
Spooner CH, *coauthor:* Rowe BH, **46(12):1380**
Spratt G & Petty TL: Partnering for optimal respiratory home care: physicians working with respiratory therapists to optimally meet respiratory home care needs, **46(5):475** *special article*
Srisuparb P, *coauthor:* Jirapaet K-S, **46(6):586**
Sriyabhaya N: Tuberculosis: a comprehensive international approach, 2nd ed, **46(10):1062** *books, films, tapes, & software*
Stern EJ: Imaging of diffuse lung disease, **46(9):948** *books, films, tapes, & software*
Stern EJ: What's new in thoracic imaging?, **46(9):911** *foreword*
Stoller JK: Are respiratory therapists effective? Assessing the evidence, **46(1):56** *lecture*
Stoller JK et al: The impact of turnover among respiratory care practitioners in a health care system: frequency and associated costs, **46(3):238** *research article*
Sui SH, *coauthor:* Han JN, **46(9):891**
Super DM, *coauthor:* Foland JA, **46(10):1019**
Suzuki R, *coauthor:* Nishiyama O, **46(7):698**
Swenson ER: Metabolic acidosis, **46(4):342** *review*

T

Takasugi JE: Case review: thoracic imaging, **46(9):949** *books, films, tapes, & software*
Tang J, *coauthor:* Siobal M, **46(10):1012**
Tasota FJ, *coauthor:* Delgado E, **46(2):185, 46(6):577**
Theodoropoulos DS: Cystic fibrosis: medical care, **46(8):832** *books, films, tapes, & software*
Thomas J, *coauthor:* Kuluz JW, **46(9):897**
Thomas PA: Evidence-based clinical practice: concepts and approaches, **46(12):1452** *books, films, tapes, & software*
Thompson W: Bone's atlas of pulmonary and critical care medicine, **46(6):622** *books, films, tapes, & software*
Thoongsuwan N: Imaging of diseases of the chest, 3rd ed, **46(9):950** *books, films, tapes, & software*
Thurman TL, *coauthor:* Holt SJ, **46(1):26**
Tonelli MR: The limits of evidence-based medicine, **46(12):1435** *conference proceedings*
Tonelli MR: Where's the evidence: debates in modern medicine, **46(12):1453** *books, films, tapes, & software*
Trent EJ, *coauthor:* Krejci CS, **46(9):932**
Turpeinen M: Nebulization of a suspension of budesonide and a solution of terbutaline into a neonatal ventilator circuit, **46(1):43** *research article*
Tyler L, *coauthor:* Schultz TR, **46(8):772**

V

VanHooser DT, *coauthor:* Christopher KL, **46(1):15**
Vaziri ND, *coauthor:* Foster GT, **46(4):384**
Votto JJ, *coauthor:* Ferranti RD, **46(8):830**

W

Wagener JS, *coauthor:* Balasubramaniam V, **46(1):68**
Waldow A, *coauthor:* Santos JWA, **46(1):53**
Warneeke EL, *coauthor:* Kallet RH, **46(1):49**
Watzman HM, *coauthor:* Schultz TR, **46(8):772**
Weavind LM: Thoracic anaesthesia: principles and practice, **46(5):495** *books, films, tapes, & software*
Webb WR, *coauthor:* Dawn SK, **46(9):912**
Wechsler RJ, *coauthor:* Nordstrom CR, **46(6):601**
White CS: Magnetic resonance imaging of the chest, **46(9):922** *review*
Wilkins RL: Measurement and evaluation in human performance, 2nd ed, **46(7):722** *books, films, tapes, & software*
Williams P, *coauthor:* Chatmongkolchart S, **46(7):666**
Winslett L, *coauthor:* Christopher KL, **46(1):15**
Woodson A, *coauthor:* Schultz TR, **46(8):772**
Wu RS-C: Drugs in anaesthetic and intensive care practice, 8th ed, **46(5):493** *books, films, tapes, & software*

Y

Yamaki K, *coauthor:* Nishiyama O, **46(7):698**
Yokoi T, *coauthor:* Nishiyama O, **46(7):698**
Young D, *coauthor:* Siobal M, **46(10):1012**
Young DA, *coauthor:* Christopher KL, **46(1):15**

Z

Zhu YJ, *coauthor:* Han JN, **46(9):891**

Subject Index to Volume 46 (2001)

1–88 JAN	297–424 APR	641–736 JUL	977–1168 OCT
89–216 FEB	425–552 MAY	737–848 AUG	1169–1238 NOV
217–296 MAR	553–640 JUN	849–976 SEP	1329–1496 DEC

A

Accidents
sleep apnea and, 1418
Acid-base
accuracy of measurements, 393
acid loading, 340
alkali loading, 337
book reviews
Fluid, electrolyte, and acid-base physiology: a problem-based approach, 3rd ed, 404
Handbook of fluid, electrolyte, and acid-base physiology: a problem-based approach, 3rd ed, 404
buffer systems, 329
disorders
case studies, 400
diagnosis, 392
dominant, identification of, 396
laboratory data, 398
simple vs. mixed, 396
disturbances, 327
fixed acids, renal excretion, 335
history, 327
hydrogen ion metabolism, 332
intracellular regulation, 333
normal composition, 336
patient management, 392
physiology, 328
renal secretion of hydrogen, 355
scales of acidity, 329
serum anion gap calculation, 395
volatile acids, pulmonary excretion, 334
Acidosis
metabolic (*See* **Metabolic acidosis**)
respiratory (*See* **Hypercapnia and hypercarbia**)
Acute respiratory distress syndrome (ARDS)
airway pressure release ventilation, with short release time, in child (case report), 1019
Cardiogenic triggering observed in a patient with acute respiratory distress syndrome (letter), 1054
evidence-based practice, 1368
fibroproliferative vs idiopathic pulmonary fibrosis (editorial), 664
low tidal volume ventilation, 142
lung collapse (case report), 49
lung collapse (letter and response), 489
protocols, 1024
lung-protective ventilation, 130
management trends, 708
pathophysiology, 131
permissive hypercapnia, 138, 160
pressure-volume curves and respiratory system mechanics, 686
steroids for (case report), 698
tracheal gas insufflation, 143
ventilator-induced lung injury, 130
Adenocarcinoma
of lung, with granular cell tumor (case report), 702
Aerosols and aerosol administration
Aerosols and the profession of respiratory care: leading the way out of the fog (letter), 275
intratracheal catheters, 194
with tracheal gas insufflation, 196
AIDS (Acquired immunodeficiency syndrome)
book review
AIDS sourcebook, 2nd ed, 952
Airway care and management. *See also* **Intubation**
evidence-based practice, 1392

Airway pressure
airway pressure release ventilation, with short release time, in pediatric ARDS (case report), 1019
high-frequency jet ventilation (letter), 826
monitoring, in tracheal gas insufflation, 187
Airway resistance
tracheostomy tube inner cannula removal, 460
Airways, artificial
unintended consequences (editorial), 1010
Allergies. *See* **Hypersensitivity**
Alveolitis, cryptogenic fibrosing. *See* **Pulmonary fibrosis**
Ambulatory care. *See* **Outpatients and outpatient care**
American Association for Respiratory Care (AARC)
Blood gas analysis and hemoximetry: 2001 revision and update (clinical practice guideline), 498
Body plethysmography: 2001 revision and update (clinical practice guideline), 506
Exercise testing for evaluation of hypoxemia and/or desaturation: 2001 revision and update (clinical practice guideline), 514
list of previously published clinical practice guidelines, 497
Methacholine challenge testing: 2001 revision and update (clinical practice guideline), 523
OPEN FORUM abstracts—2001, 1065
Static lung volumes: 2001 revision and update (clinical practice guideline), 531
2000 Donald F Egan scientific lecture, 56
American College of Chest Physicians
Roger C Bone Memorial Lecture, 267
Ammonium
excretion in metabolic alkalosis, 357
Anesthesia and anesthetics
book reviews
Drugs in anaesthetic and intensive care practice, 8th ed, 493
Thoracic anaesthesia: principles and practice, 495
Angiography
pulmonary, with computed tomography, 915
Animal models
tracheal gas insufflation, 149
Anticholinergic drugs
for acute asthma, evidence-based practice, 1382
Aorta
magnetic resonance imaging, 925
multidetector-row spiral computed tomography, 918
thoracic sonography, 934
Aortic dissection
ultrasonography, 936
Apnea. *See also* **Sleep apnea**
in tracheal gas insufflation, 120
ARDS. *See* **Acute respiratory distress syndrome (ARDS)**
Arterial blood gases
blood gas analysis and hemoximetry: 2001 revision and update (AARC clinical practice guideline), 498
hydrogen ion metabolism, 332
pH vs nanomoles per liter, 329
sampling limitations, 337
scales of acidity, 329
Arterial catheterization. *See* **Catheterization, arterial**
Arterial occlusive diseases
Allen's test: fact or myth? (letter), 274
radial lines and sticks, risks of (editorial), 229
Aspiration
assessment of, colored dye vs videofluoroscopy, 243
Asthma
acute
emergency care, 1381
evidence-based treatment, 1380
book review
Evidence-based asthma management, 1307
hypercapnia in, 376
quality of life questionnaires, 1246
Atelectasis
lung collapse during low tidal volume ventilation in ARDS (case report), 49
Atresia, bronchial
congenital, with relapsing pulmonary infection (case report), 601

B

Barotrauma
in mechanical ventilation, 130
Bartter's syndrome
metabolic acidosis, 363
Bench evaluations
Device evaluation: a critique (letter), 273
inspiratory rise time, inspiration termination criteria, in mechanical ventilators, 666
noninvasive positive pressure ventilators, for heliox delivery, 248
tracheal gas insufflation with flow relief valve, effects on delivered tidal volume, total PEEP, and carbon dioxide elimination, 577
tracheostomy tube inner cannula removal, and work of breathing, 460
Beta agonists
for acute asthma, evidence-based practice, 1381
Bicarbonates
as acid-base buffers, 329
contraindicated in primary hypercapnia, 377
for metabolic ketoacidosis, 350
Blood gases
Blood gas analysis and hemoximetry: 2001 revision and update (AARC clinical practice guideline), 498

book review
All you really need to know to interpret arterial blood gases, 2nd ed, 71
Book reviews
Advances in cardiopulmonary rehabilitation, 834
AIDS sourcebook, 2nd ed, 952
Allergic diseases: diagnosis and treatment, 2nd ed, 624
All you really need to know to interpret arterial blood gases, 2nd ed, 71
Basic mathematics for the health-related professions, 1059
Bone's atlas of pulmonary and care medicine, 622
Cardiopulmonary anatomy and physiology, 1060
Cardiopulmonary system, 69
Case review: thoracic imaging, 949
Chest radiology companion, 948
Chronic lung disease in early infancy, 829
Clinical practice in respiratory care, 282
A clinician's guide to tuberculosis, 1060
Comprehensive respiratory medicine, 279
Cystic fibrosis: medical care, 832
Decisions and evidence in medical practice: applying evidence-based medicine to clinical decision making, 1305
A dream of the heart: the life of John H Gibbon Jr, father of the heart-lung machine, 203
Drugs in anaesthetic and intensive care practice, 8th ed, 493
Entry level respiratory therapist exam guide, 3rd ed, 1057
Evidence-based asthma management, 1307
Evidence-based clinical practice: concepts and approaches, 1452
Evidence-based medicine: how to practice and teach EMB, 2nd ed, 1306
Fluid, electrolyte, and acid-base physiology: a problem-based approach, 3rd ed, 404
Fraser and Paré's diagnosis of diseases of the chest, 4th ed, 278
Fungal diseases of the lung, 3rd ed, 623
The haemodynamic effects of nitric oxide, 494
Handbook of fluid, electrolyte, and acid-base physiology: a problem-based approach, 3rd ed, 404
Handbook of hemodynamic monitoring, 67
Handbook of pediatric intensive care, 3rd ed, 493
Hyperbaric facility safety: a practical guide, 406
Hyperbaric medicine practice, 2nd ed, 405
Imaging of diffuse lung disease, 948
Imaging of diseases of the chest, 3rd ed, 950
Informatics for healthcare professionals, 1455
Interstitial lung disease, 3rd ed, 408
Interventional pulmonology, 200
Introduction to research in the health sciences, 4th ed, 1307
Irwin and Rippe's intensive care medicine, 4th ed, 491
Kendig's disorders of the respiratory tract in children, 6th ed, 68
Lecture notes on respiratory medicine, 5th ed, 68
Lung function tests: physiological principles and clinical applications, 70
Measurement and evaluation in human performance, 2nd ed, 722
Medicine meets virtual reality 2000. Envisioning healing: interactive technology and the patient-practitioner dialogue, 1309
Mosby's diagnostic and laboratory test reference, 4th ed, 200
The multiskilled respiratory therapist: a competency-based approach, 1057
Outcome of the critically ill: medicine, surgery and trauma, 1454
Pathology for the health-related professions, 2nd ed, 1058
Pharmacology for health professionals, 952
Pocket companion for critical care nursing, 202
Principles and practice of sleep medicine, 3rd ed, 625
Principles of exercise testing and interpretation, including pathophysiology and clinical applications, 3rd ed, 721
Principles of physiology, 3rd ed, 719
Procedures and techniques in intensive care medicine, 2nd ed, 491
Pulmonary diseases, 622
Pulmonary pathophysiology, 720
Pulmonary physiology, 5th ed, 721
Pulmonary rehabilitation: guidelines to success, 3rd ed, 833
Quick reference to critical care, 953
Rapid interpretation of ventilator waveforms, 201
Respiratory care equipment, 2nd ed, 951
Respiratory care exam review, 1057
Respiratory & pulmonary medicine: July 2000-June 2001: an Internet resource guide, 1456
Say It in Spanish: a guide for health care professionals, 1063
Skin signs of systemic disease, 3rd ed, 409
Studying a study and testing a test: how to read the medical evidence, 1451
Super searchers on health & medicine: the online secrets of top health & medical researchers, 1309
Textbook of critical care, 4th ed, 281
Textbook of respiratory medicine, 3rd ed, 280
Thoracic anaesthesia: principles and practice, 495
Tuberculosis: a comprehensive international approach, 2nd ed, 1062
Users' guide to the medical literature: a manual for evidence-based clinical practice, 1450

Users' guide to the medical literature: essentials of evidence-based clinical practice, 1450
Voices and choices: young people who use assisted ventilation: bibliography and analysis of the literature, 830
Voices and choices: young people who use assisted ventilation: their health and social care, and education, 830
Where's the evidence: debates in modern medicine, 1453
Bronchial diseases and disorders
congenital bronchial atresia, with relapsing pulmonary infection (case report), 601
Bronchodilators, bronchodilatation and bronchodilator administration
for COPD, 809, 815, 1295
Bronchopulmonary dysplasia
airway suctioning frequencies, very-low-birthweight mechanically ventilated infants, 783
Budesonide
nebulized, in neonatal ventilator circuits, 43

C

Carbon dioxide
elimination in tracheal gas insufflation, 153, 159, 188
in respiratory acidosis, 370
tracheal gas insufflation with flow relief valve, effects on, bench study, 577
Cardiovascular physiology
Cardiogenic triggering observed in a patient with acute respiratory distress syndrome (letter), 1054
Cardiovascular system
book reviews
Cardiopulmonary anatomy and physiology, 1060
Cardiopulmonary system, 69
Case reports
airway pressure release ventilation with short release time, in pediatric ARDS, 1019
congenital bronchial atresia, with relapsing pulmonary infection, 601
granular cell tumor with adenocarcinoma of lung, 702
low-dose methylprednisolone, for idiopathic pulmonary fibrosis, 698
lung collapse during low tidal volume ventilation in ARDS, 49
patient-ventilator interactions, in volume-support ventilation, 255
pneumonitis, from self-administration of ink solvent, 53
tracheal-innominate artery fistula from endotracheal tube tip, 1012
weaning to extubation from high-frequency oscillatory ventilation, in infant, 263
Catheterization, arterial
Allen's test (letter), 274
radial lines and sticks, risks of (editorial), 229
Catheters
bidirectional, 183
intratracheal, for drug delivery, 193
LaBrune-Boussignac tube, 181
reverse-thrust, 181
specialized, 180
for tracheal gas insufflation, 177
transtracheal oxygen, 179
Central nervous system
in respiratory alkalosis, 387
Cerebrovascular accidents. *See* **Stroke**
Certification
tracheal intubation
editorial, 227
skills retention and retraining, 234
Chest compression, high pressure
for secretion clearance, evidence-based practice, 1285
Chest imaging
advances in, 911
book reviews
Case review: thoracic imaging, 949
Chest radiology companion, 948
Imaging of diffuse lung disease, 948
Imaging of diseases of the chest, 3rd ed, 950
magnetic resonance imaging, 922
multidetector-row spiral computed tomography, 912
single-photon emission computed tomography (SPECT), 940
thoracic sonography, 932
Chest physical therapy
for secretion clearance, evidence-based practice, 1279
Children
health-related quality of life assessment, 1243
noninvasive positive pressure ventilation, lack of data on (letter), 276
weaning from ventilator, protocol- vs physician-directed, 772
Chloride deficiency
in metabolic alkalosis, 356
Chronic obstructive pulmonary disease (COPD)
acute-on-chronic ventilatory failure, management of, 713
evidence-based practice, 1204, 1294
international guidelines (editorial), 768
international guidelines (GOLD)
definition and classification, 800
epidemiology, 802
executive summary, 798
future research, 817
management, 804
pulmonary rehabilitation and quality of life, 595
respiratory acidosis in, 374

transtracheal augmented ventilation for, 15
volume-support ventilation, asynchrony and tidal volume instability (case report), 255
Clinical decision making. *See* **Decision support techniques**
Clinical Practice Guidelines (CPG). *See* **Guidelines, recommendations, and statements**
Computed tomography (CT). *See* **Tomography, computed**
Conference proceedings
evidence-based medicine, 1200
acute asthma, 1380
acute respiratory distress syndrome, 1368
airway management, 1392
chronic obstructive pulmonary disease, 1294
clinical decision making, 1442
evaluative methods, 1226
foreword, 1200
limits of, 1435
outcomes research, 1215
overview, 1201
pneumococcal vaccination, 1258
quality of life assessment, 1236
secretion clearance techniques, 1276
sleep apnea, 1418
weaning from mechanical ventilation, 1408
tracheal gas insufflation, 118
animal and lung model studies, 149
catheters for, 177
catheters for drug delivery, 193
clinical studies, 158
complications, 167
foreword, 118
monitoring and humidification, 185
obstacles to clinical implementation, 198
techniques, 119
ventilator-induced lung injury, 130
Continuous positive airway pressure (CPAP)
for sleep apnea, 1418
COPD. *See* **Chronic obstructive pulmonary disease (COPD)**
Corrections
Corrected location of author in: Aerosols and the profession of respiratory care: leading the way out of the fog, 275, (correction 496)
Corticosteroids. *See* **Steroids**
Cost-effectiveness and cost issues
respiratory care practitioner turnover, 238
Critical care. *See* **Intensive care**
Cystic fibrosis
book review
Cystic fibrosis: medical care, 832
transtracheal augmented ventilation, 15

D

Decision support techniques
for capital purchases, 1038
in evidence-based medicine, 1201, 1226, 1442
outcomes research, 1215
Delivery of health care
pneumococcal vaccination, evidence-based medicine, 1258
Diarrhea
in hyperchloremic metabolic acidosis, 347, 363
Diuretics
in metabolic alkalosis, 362
Donald F Egan Scientific Lecture
Are respiratory therapists effective? Assessing the evidence, 56
Drainage
for secretion clearance, evidence-based practice, 1283
Drugs and drug therapy
for acute asthma, evidence-based practice, 1380
book reviews
Drugs in anaesthetic and intensive care pratice, 8th ed, 493
Pharmacology for health professionals, 952
causing respiratory alkalosis, 387
intratracheal catheters, 193
Dyes
vs videofluoroscopy, for aspiration assessment in tracheostomy patients, 243
Dysphagia
stroke-induced, electrical stimulation for, 466
Dyspnea and dyspnea assessment
patient-ventilator discoordination, 1031

E

Economic aspects of illness and health care
home respiratory care reimbursement, 477
Editorials
Acute exacerbation of idiopathic pulmonary fibrosis and fibroproliferative acute respiratory distress syndrome: similar disease, similar treatment? 664
Dual control modes, closed loop ventilation, handguns, and tequila, 232
Evidence-based medicine in respiratory care, 1200
New international guidelines for chronic obstructive pulmonary disease, 768
Radial arterial lines and sticks: what are the risks? 229
Tracheal intubation: training and retention, 227
Unintended consequences of artificial airways, 1010
Ventilator circuit changes: "wu wei" may save time, labor, and money, 888

Education, patient
for COPD, 809
Education and training
tracheal intubation (editorial), 227
Electric stimulation
for stroke-induced swallowing disorders, 466
Embolism, pulmonary. *See* **Pulmonary embolism**
Emergency care
acute asthma, 1381
airway management, evidence-based, 1392
Endotracheal tubes. *See* **Tubes, endotracheal**
End-tidal CO_2. *See* **Carbon dioxide**
Equipment and supplies
book review
Respiratory care equipment, 2nd ed, 951
chemically-reactive heated humidifier, 37
Device evaluation: a critique (letter), 273
Siemens Servo 300A ventilator. Automode evaluation, 26
ventilator purchase, decision analysis, 1038
ventilator reliability, failure time analysis of 5 brands, 789
Evaluation studies
book review
Measurement and evaluation in human performance, 2nd ed, 722
mechanical ventilation innovations, 267
ventilator reliability, failure time analysis of 5 brands, 789
Evidence-based medicine
acute asthma, 1380
acute respiratory distress syndrome, 1368
airway management, 1392
book reviews
Decisions and evidence in medical practice: applying evidence-based medicine to clinical decision making, 1305
Evidence-based clinical practice: concepts and approaches, 1452
Evidence-based medicine: how to practice and teach EMB, 2nd ed, 1306
Studying a study and testing a test: how to read the medical evidence, 1451
Users' guide to the medical literature: a manual for evidence-based clinical practice, 1450
Users' guide to the medical literature: essentials of evidence-based clinical practice, 1450
Where's the evidence: debates in modern medicine, 1453
chronic obstructive pulmonary disease, 1294
clinical decision-making, 1442
clinical research and clinical practice relationships, 1435
conceptual errors, 1435
conference proceedings, 1200, 1368
evaluative methods, 1226
evidence
grading, 1442
hierarchy of, 1369
sources, 1206
history, 1201
limits of, 1435
outcomes research, 1215
pneumococcal vaccination, 1258
as problem-solving strategy, 1201
quality of life assessment, 1236
randomized controlled trials, history of, 1201
in respiratory care (editorial), 1200
secretion clearance techniques, 1276
sleep apnea, 1418
weaning from mechanical ventilation, 1408
Web site reviews, 1311
Examinations and quizzes
book reviews
Entry level respiratory therapist exam guide, 3rd ed, 1057
Respiratory care exam review, 1057
Exercise testing
book review
Principles of exercise testing and interpretation, including pathophysiology and clinical applications, 3rd ed, 721
Exercise testing for evaluation of hypoxemia and/or desaturation: 2001 revision and update (AARC clinical practice guideline), 514
Expectorants
for COPD, evidence-based practice, 1297
Extracorporeal membrane oxygenation (ECMO)
book review
A dream of the heart: the life of John H Gibbon Jr, father of the heart-lung machine, 203

F

Fluids and secretions
retention, in low tidal volume ventilation in ARDS (case report), 49
secretion clearance techniques, evidence-based, 1276
Fluoroscopy
video vs colored dyes, for aspiration assessment in tracheostomy, 243
Flutter therapy
for secretion clearance, evidence-based practice, 1283
Fraction of inspired oxygen (F_{IO_2})
via nasal cannula in infants, safety of, 897
Fungal infections
book review
Fungal diseases of the lung, 3rd ed, 623

G

Gitelman's syndrome
metabolic acidosis, 363
Glomerular filtration rate
in metabolic acidosis, 356
Granular cell tumor
with adenocarcinoma of lung (case report), 702
Guidelines, recommendations, and statements
Blood gas analysis and hemoximetry: 2001 revision and update (AARC clinical practice guideline), 498
Body plethysmography: 2001 revision and update (AARC clinical practice guideline), 506
Cardiopulmonary resuscitation and emergency cardiovascular care. American Heart Association (editorial), 227
chronic obstructive pulmonary disease (GOLD), executive summary, 798
Exercise testing for evaluation of hypoxemia and/or desaturation: 2001 revision and update (AARC clinical practice guideline), 514
list of previously published, AARC clinical practice guidelines, 497
Methacholine challenge testing: 2001 revision and update (AARC clinical practice guideline), 523
New international guidelines for chronic obstructive pulmonary disease (editorial), 768
Static lung volumes: 2001 revision and update (AARC clinical practice guideline), 531

H

Heat and moisture exchangers. *See also* **Humidifiers and humidification**
chemically-reactive, clinical trials, 37
Helium-oxygen gas mixture
with noninvasive positive pressure ventilation, 248
Hemodynamics, pulmonary
book review
Handbook of hemodynamic monitoring, 67
Home care
allocation of resources, 480
benefits, 482
reimbursement, 477
respiratory
conditions requiring, 476
patient monitoring, 478
physician/respiratory therapist partnerships, 475
Humidifiers and humidification. *See also* **Heat and moisture exchangers**
chemically-reactive heated, clinical trial, 37
in tracheal gas insufflation, 173, 185
Hydrogen
renal secretion of, 355
Hydrogen ion concentration (pH). *See* **Arterial blood gases**
Hyperbaric oxygenation
book reviews
Hyperbaric facility safety: a practical guide, 406
Hyperbaric medicine practice, 2nd ed, 405
Hypercapnia and hypercarbia
alkali therapy, 377
assessment, 373, 376
outpatient evaluation, 378
pathophysiology, 367
permissive, 138, 160, 376, 708
respiratory dead space, 371
review, 366
signs and symptoms, 371
treatment, 377
ventilatory support, 378
worsening of, in oxygen therapy, 375
Hypersensitivity
book review
Allergic diseases: diagnosis and treatment, 2nd ed, 624
Hypertension
in metabolic alkalosis, 362
pulmonary (*See* **Pulmonary hypertension**)
sleep apnea in, 1418
Hyperventilation
syndrome, in respiratory alkalosis, 388
vs high-frequency flow interruption ventilation, in pulmonary hypertension of newborn, 586
Hypothermia
chemically-reactive heated humidifiers, clinical trial, 37
Hypoventilation
alveolar, 370
in obesity, 375
Hypoxemia and hypoxia
Exercise testing for evaluation of hypoxemia and/or desaturation: 2001 revision and update (AARC clinical practice guideline), 514
permissive, in ARDS management, 710
in respiratory alkalosis, 386
transtracheal augmented ventilation, 15

I

Infants. *See also* **Neonatal disease and disorders** *and* **Respiratory care, neonatal**
fraction of inspired oxygen via nasal cannula, safety of, 897
Inflammation and inflammatory mediators
in ventilator-induced lung injury, 136

Innominate artery
tracheal-innominate artery fistula caused by (case report), 1012
Inservice training
costs, and respiratory care practitioner turnover, 238
Insufflation, tracheal gas
in acute respiratory distress syndrome, 130
animal and lung model studies, 149
carbon dioxide elimination, 153, 159, 188
catheters, 177
clinical studies, 158
complications, 164, 167
airway trauma, 174
altered airway pressures and volumes, 168
humidification, 173
tracheal gas exsufflation, 170
ventilator triggering, 172
conference proceedings, 118
in end-stage pulmonary disease, 159
with flow relief valve, effects on delivered tidal volume, total PEEP, and CO_2 elimination, bench study, 577
humidification, 185
intratracheal catheters for drug delivery, 193
lung mechanics, 149
during mechanical ventilation, 160
monitoring, 152, 164, 175, 185
obstacles to clinical implementation, 198
physiologic effects, 159
techniques, 119, 126
continuous oxygen insufflation, 120
high frequency jet ventilation, 125
high frequency jet ventilation (letter), 826
intratracheal pulmonary ventilation, 125
transtracheal jet ventilation, 123
transtracheal oxygen administration, 123
tidal volume, 153
ventilation in, 153
ventilator-induced lung injuries, 130
ventilator interactions, 153
Intensive care
book reviews
Drugs in anaesthetic and intensive care practice, 8th ed, 493
Handbook of pediatric intensive care, 3rd ed, 493
Irwin and Rippe's intensive care medicine, 4th ed, 491
Outcome of the critically ill: medicine, surgery and trauma, 1454
Procedures and techniques in intensive care medicine, 2nd ed, 491
Quick reference to critical care, 953
Textbook of critical care, 4th ed, 281
Intensive care unit (ICU)
respiratory therapist effectiveness in, 56
Internet
book reviews
Informatics for healthcare professionals, 1455
Medicine meets virtual reality 2000. Envisioning healing: interactive technology and the patient-practitioner dialogue, 1309
Respiratory & pulmonary medicine: July 2000–June 2001: an Internet resource guide, 1456
Super searchers on health & medicine: the online secrets of top health & medical researchers, 1309
Web site reviews
evidence-based medicine, online resources, 1311
MD Consult, 411
Interstitial lung disease
book review
Interstitial lung disease, 3rd ed, 408
methylprednisolone in acute exacerbation of idiopathic pulmonary fibrosis (case report), 698
transtracheal augmented ventilation for, 15
Intubation. *See also* **Airway care and management**
intratracheal pulmonary ventilation, 125
tracheal
complications, 227
recertification and skill retention, 234
training for (editorial), 227
unintended consequences (editorial), 1010

J

Jet ventilation
high frequency, 125
transtracheal, 123
Job skills
tracheal intubation, skills retention and retraining, 234

K

Kidney tubules
bicarbonate resorption, 355
metabolic acidosis, 347
Kyphosis
transtracheal augmented ventilation for, 15

L

Laboratories and laboratory practice
book review
Mosby's diagnostic and laboratory test reference, 4th ed, 200
Lactic acidosis. *See* **Metabolic acidosis**
Letters to the editor
Aerosols and the profession of respiratory care: leading the way out of the fog, 275

Allen's test: fact or myth?, 274
Cardiogenic triggering observed in a patient with acute respiratory distress syndrome, 1054
Device evaluation: a critique, 273
The future of respiratory care, 1304
High-frequency jet ventilation, 826
The lack of data on off-label use of noninvasive positive pressure ventilation in children, 276
Lung collapse during low tidal volume ventilation in acute respiratory distress syndrome (letter and response), 489
A useful oxygen dilution formula, 1055
Weaning parameters: who cares! (letter and response), 946

Lung
book reviews
Pulmonary physiology, 5th ed, 721
collapse, during low tidal volume ventilation, in ARDS (case report), 49
tracheal gas insufflation models, 149

Lung cancer
magnetic resonance imaging, 926

Lung diseases and disorders
book reviews
Bone's atlas of pulmonary and care medicine, 622
Chronic lung disease in early infancy, 829
Imaging of diffuse lung disease, 948
Pulmonary diseases, 622
Pulmonary pathophysiology, 720
cystic, with persistent air leak, ventilator weaning in (case report), 263
end-stage, tracheal gas insufflation for, 159
fraction of inspired oxygen via nasal cannula, in infants, safety of, 897
granular cell tumor with adenocarcinoma of lung (case report), 702
inspiratory rise time and inspiration termination criteria, in mechanical ventilators, 666
mean alveolar pressure during constant-flow and constant-pressure inflation, 678
multidetector-row spiral computed tomography, 912
parenchymal, in respiratory alkalosis, 386
thoracic sonography for, 935

Lung injuries
low tidal volume ventilation protocols, in acute lung injury or ARDS, 1024
permissive hypercapnia in ventilation, 138
ventilator-induced, protective strategies in ARDS, 130, 1370

Lung volumes
Static lung volumes: 2001 revision and update (AARC clinical practice guideline), 531

M

Magnesium sulfate
for acute asthma, evidence-based practice, 1383

Magnetic resonance imaging (MRI)
of chest, 922
ventilation, 930

Mathematics
book review
Basic mathematics for the health-related professions, 1059

Measurement and measurement techniques
health-related quality of life instruments, 1236

Mechanical ventilation
in acute respiratory distress syndrome, 130
airway pressure release ventilation, with short release time, pediatric (case report), 1019
cardiogenic triggering (letter), 1054
evidence-based approach, 1370
lung collapse in low tidal volume ventilation (letter and response) 489
pressure-volume curves, 686
for acute respiratory failure, history, 707
airway management, evidence-based, 1392
airway suctioning frequencies, very-low-birthweight infants, 783
Automode evaluation, with Siemens Servo 300A ventilator, 26
book reviews
Rapid interpretation of ventilator waveforms, 201
Voices and choices: young people who use assisted ventilation: bibliography and analysis of the literature, 830
Voices and choices: young people who use assisted ventilation: their health and social care, and education, 830
in chronic obstructive pulmonary disease, 815
classification and terminology, 604
closed loop, evaluation (editorial), 232
high-frequency flow interruption ventilation vs hyperventilation, in pulmonary hypertension of newborn, 586
high-frequency jet ventilation (letter), 826
innovations, 267
inspiratory rise time, inspiration termination criteria, 666
low tidal volume protocols, in acute lung injury or ARDS, 1024
lung injuries form, 130
mean alveolar pressure, in constant-flow and constant-pressure lung inflation, 678
noninvasive positive pressure
in children, lack of data on (letter), 276
heliox delivery, 248
nocturnal, for COPD, evidence-based practice, 1298

respiratory acidosis, 378
respiratory alkalosis, 387
tracheal gas insufflation, 160
ventilator purchase, decision analysis, 1038
ventilator reliability, failure time analysis of 5 brands, 789
volume-support, asynchrony and tidal volume instability (case report), 255
weaning
in children, protocol- vs physician-directed, 772
evidence from clinical research, 1408
factors in, 28
from high-frequency oscillatory, in infant (case report), 263
measurements of oxygen cost of breathing in trials of, 902
predictors, 1412
spontaneous breathing trials, 1411
with tracheal gas insufflation, 163
tracheostomy tube inner cannula removal, 460
Weaning parameters: who cares! (letter and response), 946
Mediastinum
magnetic resonance imaging, 927
Medical informatics
book review
Informatics for healthcare professionals, 1455
Meta-analysis
in evidence-based medicine, 1232
Metabolic acidosis
acid load response, 343
chemical buffering, 343
consequences, 344
diagnosis, 344
etiology, 344
high anion gap, 348
hyperchloremic, 347
ketoacidosis, 349
lactic, 348, 386
pathophysiology, 342
permissive hypercapnia, 138
renal compensation, 344
treatment, 350
Metabolic alkalosis
effects of, 363
gastric, 360
mineralocorticoid excesses, 362
overview, 354
pathophysiology, 355
respiratory compensation, 363
treatment, 364
Metabolic disorders
acid-base disturbances, 327
causing respiratory alkalosis, 387
Methacholine
Methacholine challenge testing: 2001 revision and update (AARC clinical practice guideline), 523
Methylprednisolone
prolonged low-dose, for idiopathic pulmonary fibrosis (case report), 698
Models, mathematical
lung, inspiratory rise time, inspiration termination criteria, in mechanical ventilators, 666
lung, mean alveolar pressure during constant-flow and constant-pressure inflation, 678
Monitoring
book review
Handbook of hemodynamic monitoring, 67
trends in, 714

N

National Institute of Biomedical Imaging and Bioengineering
establishment of, 911
Nebulizers, inhalers, and vaporizers
Aerosols and the profession of respiratory care: leading the way out of the fog (letter), 275
budesonide and terbutaline delivery, in neonatal ventilation, 43
Neonatal diseases and disorders
pulmonary hypertension of newborn, high-frequency flow interruption ventilation and hyperventilation compared, 586
Nitric oxide
book review
The haemodynamic effects of nitric oxide, 494
inhaled, in ARDS management, 1371
Nurses and nursing
book review
Pocket companion for critical care nursing, 202

O

Obesity
hypoventilation syndrome, 375
Oleic acid
experimental lung injury, pressure-volume curves, 686
Open Forum
abstracts—2001, 1065
Outcome assessment
history of, 1216
in respiratory care, 1215
terminology, 1216
Outpatients and outpatient care
respiratory therapist effectiveness, 56

Oxygen
cost of breathing, in mechanical ventilation weaning, 902
Oxygen administration and therapy
for chronic obstructive pulmonary disease, 815, 1297
continuous insufflation, 120
nocturnal, 15
oxygen dilution formula (letter), 1055
transtracheal, 15, 123
via nasal cannula, fraction of inspired oxygen in infants, safety of, 897
worsening hypercapnia in, 375
Oxygenation
apneic, 120
Oxygen delivery systems
with heliox mixtures, 248
nasal cannula, in infants, fraction of inspired oxygen, safety issues, 897

P

Pathology and pathophysiology
book review
Pathology for the health-related professions, 2nd ed. 1058
Patient care
clinical decision-making, 1442
Patient compliance
in home respiratory care, 480
Patient positioning
prone, in ARDS management, 1371
Peak airway pressure. *See* **Airway pressure**
Personnel
respiratory care practitioner turnover, 238
Petroleum
distillates, pneumonitis from self-administration (case report), 53
pH. *See* **Arterial blood gases**
Pharmacology. *See* **Drugs and drug therapy**
Physiology
book review
Principles of physiology, 3rd ed, 719
Plethysmography
Body plethysmography: 2001 revision and update (AARC clinical practice guideline), 506
Pleural diseases and disorders
thoracic sonography, 933
Pneumococcal infections
vaccination, evidence-based medicine, 1258
Pneumonia
from self-administered I.V. ink solvent (case report), 53
Pneumonia, ventilator-associated
airway management, evidence-based, 1392
diagnostic criteria, 892
microbial culture techniques, evidence-based comparison, 1404
ventilator circuit change, frequency and risk of, 891
ventilator circuit change, frequency and risk of (editorial), 888
Pneumonitis. *See* **Pneumonia**
Pneumothorax
with cystic lung disease, ventilator weaning to extubation in infant (case report), 263
Poisoning and toxicity
ink solvent, pneumonitis from self-administered I.V. (case report), 53
Polysomnography
sleep apnea diagnosis, 1418
Positive end-expiratory pressure (PEEP)
Automode evaluation, with Siemens Servo 300A ventilator, 26
low tidal volume ventilation protocols, in acute lung injury or ARDS, 1024
lung collapse during low tidal volume ventilation in ARDS (case report), 49
monitoring, in tracheal gas insufflation, 187
pressure-volume curves, in experimental ARDS, 686
in tracheal gas insufflation, 170
tracheal gas insufflation with flow relief valve, effects on, bench study, 577
in ventilator-induced lung injury, 136
weaning children from ventilator, protocol- vs physician-directed, 772
Positive expiratory pressure
for secretion clearance, evidence-based practice, 1283
Positive-pressure ventilation. *See* **Mechanical ventilation**
Postoperative complications
volume-support ventilation, asynchrony and tidal volume instability (case report), 255
Potassium
excretion in metabolic alkalosis, 356
Premature infants
airway suctioning frequencies, very-low-birthweight mechanically ventilated infants, 783
Problem solving
in evidence-based medicine, 1201
Professional practice
innovations in mechanical ventilation, 267
Protocols
low tidal volume ventilation, in acute lung injury or ARDS, 1024
ventilator weaning, 772, 905, 1413
Weaning parameters: who cares! (letter and response), 946
Pulmonary arteries and veins
magnetic resonance imaging, 924

Pulmonary embolism
recurrent, transtracheal augmented ventilation, 15
single-photon emission computed tomography, 940
ultrasonography, 935
Pulmonary fibrosis, idiopathic
low-dose methylprednisolone for (case report), 698
vs fibroproliferative acute respiratory distress syndrome (editorial), 664
Pulmonary function testing
book reviews
Interventional pulmonology, 200
Lung function tests: physiological principles and clinical applications, 70
pressure-volume curves, in experimental ARDS, 686
Pulmonary hypertension of newborn
high-frequency flow interruption ventilation vs hyperventilation, 586
Pulmonary infections
relapsing, with bronchial atresia (case report), 601
Purchasing
capital purchases, decision analysis for, 1038

Q

Quality of health care
home respiratory care, 483
quality of life and, 1236
respiratory therapists, effectiveness of, 56
Quality of life
in children, 1243
health-related, assessment of, 1236
pulmonary rehabilitation programs improving, 595
sleep apnea and, 1418

R

Radial artery
Allen's test: fact or myth? (letter), 274
lines and sticks, risks of (editorial), 229
Randomized controlled trials
chronic obstructive pulmonary disease, 1204
in evidence-based medicine, 1231
thrombolytic therapy, 1202
Rehabilitation, pulmonary
book reviews
Advances in cardiopulmonary rehabilitation, 834
Pulmonary rehabilitation: guidelines to success, 3rd ed, 833
for COPD, 812, 1298
exercise session staffing, 694
quality of life and, 595
Research
book reviews
Introduction to research in the health sciences, 4th ed, 1307
Super searchers on health & medicine: the online secrets of top health & medical researchers, 1309
innovations in mechanical ventilation, 267
relationship between clinical research and clinical practice, 1435
Research methods
Device evaluation: a critique (letter), 273
Respiration
breathing patterns, classification of, in mechanical ventilation, 604
Respiratory acidosis. *See* **Hypercapnia and hypercarbia**
Respiratory alkalosis
classification, 385
defined, 385
diagnosis, 389
electrolyte hemostasis, 386
etiology, 386
lactic acidosis, 386
metabolic acidosis and, 348
pathophysiology, 385
review of, 384
systemic effects, 388
therapeutic uses, 389
treatment, 389
Respiratory care
book reviews
Clinical practice in respiratory care, 282
Lecture notes on respiratory medicine, 5th ed, 68
The multiskilled respiratory therapist: a competency-based approach, 1057
future of (special article), 705; (letter), 1304
history, 705
home-based, physician/respiratory therapist partnerships, 475
mechanical ventilation innovations, 267
terminology, 705
trends, 705
Respiratory care, neonatal
airway suctioning frequencies, in very-low-birthweight, 783
book review
Chronic lung disease in early infancy, 829
nebulized budesonide and terbutaline in ventilator circuits, 43
Respiratory care, pediatric
airway pressure release ventilation, with short release time, in ARDS (case report), 1019
book reviews
Handbook of pediatric intensive care, 3rd ed, 493

Kendig's disorders of the respiratory tract in children, 6th ed, 68
fraction of inspired oxygen via nasal cannula, in infants, safety of, 897
lack of data on off-label use of noninvasive positive pressure ventilation (letter), 276
weaning from ventilator, protocol- vs physician-directed, 772
weaning to extubation from high-frequency oscillatory ventilation, 263
RESPIRATORY CARE Journal
history of, 717
Respiratory diseases and disorders
book reviews
Comprehensive respiratory medicine, 279
Fraser and Paré's diagnosis of diseases of the chest, 4th ed, 278
Textbook of respiratory medicine, 3rd ed, 280
Respiratory insufficiency
asynchrony and tidal volume instability in volume-support ventilation (case report), 255
Respiratory syncytial virus infections
airway pressure release ventilation for in ARDS (case report), 1019
Respiratory therapists
effectiveness, 56
history, 714
tracheal intubation
recertification and skills retention, 234
training (editorial), 227
turnover, frequency and costs of, 238
Risk factors
radial arterial lines and sticks (editorial), 229
Roger C Bone Memorial Lecture
innovations in mechanical ventilation, 267
Rural health
pneumococcal vaccination, evidence-based medicine, 1258

S

Scintigraphy
quantitative lung scan, 941
Secretions. *See* **Fluids and secretions**
Sleep apnea. *See also* **Apnea**
obstructive, evidence-based medicine, 1418
quality of life index, 1248
Sleep disorders
book review
Principles and practice of sleep medicine, 3rd ed, 625
quality of life questionnaires, 1248
Solvents
pneumonitis from self-administration of I.V. ink (case report), 53
Sonography
thoracic, 932
Spanish language
book review
Say it in Spanish: a guide for health care professionals, 1063
SPECT. *See* **Tomography, computed**
Staffing and scheduling
pulmonary rehabilitation exercise sessions, 694
Steroids
for acute asthma, evidence-based practice, 1383
for COPD, 768, 811, 1297
for idiopathic pulmonary fibrosis and ARDS (editorial), 664
late phase, for ARDS, 1372
Stroke
electrical stimulation for swallowing disorders, 466
Suction and suctioning devices
airway suctioning frequencies, very-low-birthweight mechanically ventilated infants, 783
Surveys and questionnaires
health-related quality of life assessment, 1236
quality of life and chronic respiratory disease, pulmonary rehabilitation improving, 595
Swallowing
assessment of, 467
disorders (*See* **Dysphagia**)
videofluoroscopy vs colored dyes, for aspiration assessment in tracheostomy, 243

T

Terbutaline
nebulized, in neonatal ventilator circuits, 43
Thoracic imaging. *See* **Chest imaging**
Thrombolytic therapy
randomized controlled trials, 1202
Tidal volume
high-frequency jet ventilation (letter), 826
instability, in volume-support ventilation (case report), 255
low
in ARDS management, 142
ventilation protocols, 1024
in ventilator-induced lung injury, 136
lung collapse in low tidal volume ventilation (letter and response), 489
pressure-volume curves, in experimental ARDS, 686
in tracheal gas insufflation, 152, 186, 577

Tomography, computed
multidetector-row spiral, for thoracic disease diagnosis, 912
single-photon emission (SPECT), of chest, 940
Tracheal gas insufflation. *See* **Insufflation, tracheal gas**
Tracheotomy and tracheostomy
aspiration assessment, colored dye vs videofluoroscopy, 243
percutaneous, 1392
tube inner cannula removal and work of breathing, 460
ventilator-associated pneumonia and, 1392
Tracheovascular fistula
tracheal-innominate artery fistula, from endotracheal tube tip (case report), 1012
Transtracheal gas insufflation. *See* **Insufflation, tracheal gas**
Transtracheal oxygen therapy. *See* **Oxygen administration and therapy, transtracheal**
Tuberculosis
book reviews
A clinician's guide to tuberculosis, 1060
Tuberculosis: a comprehensive international approach, 2nd ed, 1062
Tubes, endotracheal
budesonide and terbutaline delivery, in neonatal ventilation, 43
inner cannula removal and work of breathing, 460
intratracheal pulmonary ventilation, 125
reverse-flow-design, 181
tracheal-innominate artery fistula caused by (case report), 1012
unintended consequences of artificial airways (editorial), 1010
Turnover, personnel
respiratory therapists, 238

U

Ultrasonography
thoracic, 932

V

Vaccination
pneumococcal, evidence-based practice, 1258
Ventilation
closed-loop (*See* **Mechanical ventilation**)
low tidal volume, lung collapse during, in ARDS (case report), 49
pressure-support, 666
in tracheal gas insufflation, 152
transtracheal, 15
volume-support, patient-ventilation interactions in (case report), 255
Ventilator circuits
frequency of changes, and ventilator-associated pneumonia, 891; (editorial), 888
neonatal, nebulized budesonide and terbutaline in, 43
Videofluoroscopy. *See* **Fluoroscopy, video**
Virtual reality
book review
Medicine meets virtual reality 2000. Envisioning healing: interactive technology and the patient-practitioner dialogue, 1309
Volutrauma
in ventilator-induced lung injury, 135

W

Weaning from ventilatory support. *See* **Mechanical ventilation, weaning**
Web site reviews. *See also* **Internet**
evidence-based medicine, online resources, 1311
MD Consult, 411
Work of breathing
Automode evaluation, with Siemens Servo 300A ventilator, 26
oxygen costs, in mechanical ventilation weaning trials, 902
in tracheal gas insufflation, 155
tracheostomy tube inner cannula removal, 460
volume-support ventilation, asynchrony and tidal volume instability (case report), 255

In-Service

AARC Can Help You Meet

It's also an ideal classroom tool for training students. Easy-to-use simulations
treatment based on the case scenarios. Each program installs easily
successfully complete scenarios can print certificates of completion

FOUR EASY WAYS TO ORDER

PHONE: (972) 243-2272 to charge your order.

ONLINE: http://store.yahoo.com/aarc/

MAIL: AARC, 11030 Ables Lane, Dallas, Texas 75229-4593

FILL OUT THIS FORM AND FAX: (972) 484-2720 or
(972) 484-6010 to charge your order.

Name Title

AARC Member Number

Company/Institution

Shipping Address

City / State / Zip + 4

Telephone (Please include area code) Fax Number (Please include area code)

Order Number	Description of Item	Qty	Price Per Item	Total Price
	ALL ORDERS MUST INCLUDE			
	SHIPPING & HANDLING			
	CHARGES			

* Texas residents add 8.25% sales tax Sales tax calculated on "Price per item" before postage is added.Texas customers exempt from sales tax must attach an exemption certificate

Sales Tax*

Shipping & Handling**

TOTAL

ORDER TOTAL	UPS GROUND	ORDER TOTAL	UPS GROUND
$15.00 or less	$4.25	$100.01 to $150.00	$10.25
$15.01 to $25.00	$5.25	$150.01 to $200.00	$12.25
$25.01 to $40.00	$6.25	$200.01 to $250.00	$14 25
$40.01 to $60.00	$7.25	$250.01 to $300.00	$16.25
$60.01 to $80.00	$8.25	$300.01 to $400.00	$18.25
$80.01 to $100.00	$9.25	$400.01 and up	$20.25

SOFTWARE SHIPS WITHIN 1-2 BUSINESS DAYS
PLEASE CALL FOR ALL OTHER SHIPPING RATES!

Chronic Obstructive Pulmonary Disease II (COPD) Clinical Simulation

This simulation begins with the user performing the initial evaluation and treatment of a patient with COPD. After appropriate oxygen therapy is initiated and the patient is stabilized, the user performs PFTs to classify the degree of pulmonary impairment. A pulmonary rehabilitation is initiated as well as recommendations regarding the cleaning of respiratory equipment at home. CAI Software. Requires Windows 3.1 or higher. 3.5" floppy PC disk.

Item PEL15 — $65.00 • Non Member $95.00
Multi-Installation Site License $65.00

Myasthenia Gravis Clinical Simulation

With this program, the user deals with the assessment and treatment of a patient with a history of myasthenia gravis. The user is required to perform preop assessment and therapy. After surgery the patient experiences respiratory distress and after evaluation by the user, recommendations are requested for her cardiopulmonary status therapy. When the patient experiences severe respiratory distress, the user performs further evaluation and places the patient on a ventilator. And, after stabilization, extubation parameters and instructions for removal from ventilation are requested. CAI Software. Requires Windows 3.1 or higher. 3.5" floppy PC disk.

Item PEL16 — $65.00 • Non Member $95.00
Multi-Installation Site License $65.00

Pediatric Asthma Clinical Simulation

The user assesses and recommends initial therapy of a pediatric patient with asthma who presents to the ER. After low flow oxygen and bronchodilator is administered, the user is required to obtain for laboratory date that results in increasing the FIO2. After transfer to the pediatric unit, the user is required to provide further assessment and recommendations for treatment. Twenty-four hours later the patient is in acute respiratory distress which requires assessment that results in mechanical ventilation. Ventilator settings are requested and assessment of the results of the ventilation is performed. CAI Software. Requires Windows 3.1 or higher. 3.5" floppy PC disk.

Item PEL17 — $65.00 • Non Member $95.00
Multi-Installation Site License $65.00

Training

Regulatory Requirements.

present case studies that require the user to perform assessment and and fast, so your students or staff are learning in no time. Users who so that you can document their activity.

Flail Chest Clinical Simulation

This simulation deals with the initial assessment and treatment of a 24-year old female entering the emergency room after being involved in an automobile accident. After stabilization, the user is required to evaluate and treat pulmonary complications. These complications lead to emergency resuscitation, intubation, and mechanical ventilation, after which a pneumothorax develops that requires the users assessment and treatment. A chest tube is inserted, and the student is asked to evaluate the information obtained by a pleurovac drainage system. CAI Software. Requires Windows 3.1 or higher. 3.5" floppy PC disk.

Item PEL18 — $65.00 • Non Member $95.00
Multi-Installation Site License $65.00

Near Drowning Clinical Simulation

This simulation presents the user with a 16-year old near drowning victim who has been administered high flow oxygen along with obtainment of an A8G. After intubation and further blood gas analysis, ventilator parameters are initiated and adjusted by the user, and the patient develops pneumonia that must be evaluated and treated. As the simulation develops, the patient is gradually weaned from the ventilator by altering the mode of ventilation as well as other ventilator parameters. CAI Software. Requires Windows 3.1 or higher. 3.5" floppy PC disk.

Item PEL19 — $65.00 • Non Member $95.00
Multi-Installation Site License $65.00

Meconium Aspiration Clinical Simulation

This program presents a c-section delivery patient for the user's initial assessment and evaluation of clinical and laboratory tests, including UAC sampling. Meconium aspiration is suspected and the user is asked to treat the progressive ventilatory deterioration. Then, a respiratory crisis occurs that requires manual resuscitation and eventual mechanical ventilation. The user then pursues the evaluation and treatments of persistent fetal circulation. CAI Software. Requires Windows 3.1 or higher. 3.5" floppy PC disk.

Item PEL20 — $65.00 • Non Member $95.00
Multi-Installation Site License $65.00

Smoke Inhalation Clinical Assessment

Presents a patient who was found unconscious in a burning building who requires initial assessment and examination for airway management and initial therapy. In addition to the burns of the upper airway, carbon monoxide poisoning is suspected and the student is required to recommend appropriate tests and suggest a course of treatment. Mechanical ventilation is initiated and hemodynamic monitoring results are made available for interpretation and to guide further therapy. CAI Software. Requires Windows 3.1 or higher. 3.5" floppy PC disk.

Item PEL21 — $65.00 • Non Member $95.00
Multi-Installation Site License $65.00

Deadspace Computer-Assisted Instruction

The program begins with a description of deadspace including the difference between anatomic and alveolar deadspace, calculations of alveoiar ventilation, and the ratio of deadspace to tidal volume. Also deals with the various causes of, and increase in the amount of deadspace. Explains the clinical evaluation and measurement of deadspace conditions and the various techniques to assist in the clinical detection, assessment and treatment of deadspace conditions. Includes a 15-question quiz. CAI Software. Requires Windows 3.1 or higher. 3.5" floppy PC disk.

Item PEL22 — $65.00 • Non Member $95.00
Multi-Installation Site License $65.00

Shunt Computer-Assisted Instruction

This program defines the shunt process along with several diagrams that illustrate the concepts of anatomic and alveolar shunting. It also describes the basic causes of an increase in the percent of shunt and its clinical diagnosis. Includes the formulas for the calculation of the percent of shunt, the classic shunt equation, several shorter equations, various techniques used in the treatment of shunt including the use of PEEP and permissive hypercapnea. 15-question quiz. CAI Software. Requires Windows 3.1 or higher. 3.5" floppy PC disk.

Item PEL23 — $65.00 • Non Member $95.00
Multi-Installation Site License $65.00

All software usually ships in 1-2 days.

RESPIRATORY THERAPIST

Spectrum Healthcare Resources, www.shrusa.com has an On-Call/ Part Time opportunity at our Naval Medical Center San Diego. **Requires Level 3 nursery** experience and current BLS, NRP, and CA RT License. 12 hour night shifts guaranteed. Excellent compensation! For immediate consideration please call Joyce Hornaday (619) 238-3609 x20; and fax or email resume to (619) 238-3551, jhornaday@spectrumhealth.com EOE/AA

Circle 105 on product information card

NEW IISP

CULTURAL COMPETENCE

Learn How to Provide Better Patient Care For All Your Patients

This IISP helps you understand the impact of different ethnic, religious, and cultural backgrounds on the delivery of patient care. Presents the importance of systematic information gathering about the literacy, family dynamics, and health beliefs of the many cultures that populate the U.S. Individual Independent Study Packet, Softcover Book.

ITEM CP2-A1
$12.00 ($16.00 nonmembers)
Add $4.25 for Shipping & Handling.

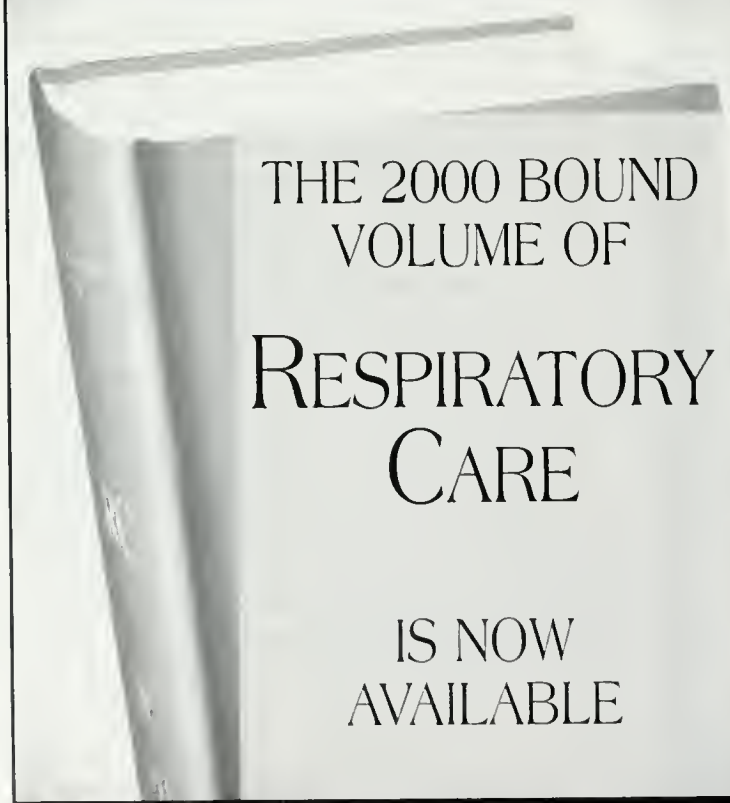
ORDER ONLINE AT:
http://store.yahoo.com/aarc

ORDER BY PHONE:
(972) 243-2272 • FAX (972) 484-2720
With MasterCard, Visa, PO

AARC

11030 Ables Lane • Dallas, TX 75229

Visit www.aarc.org
for all your respiratory information needs.



THE 2000 BOUND VOLUME OF

RESPIRATORY CARE

IS NOW AVAILABLE

Volume 45 is bound in a blue-buckram cover and may be imprinted, free of charge, with your name or the name of your organization. Each volume is $40 for current AARC members and $80 for non-members. Shipping is included for U.S. and Canadian residents.

Available for a limited time, older bound volumes at discounted rates.

ORDERS MUST BE PREPAID—INCLUDE CHECK, INSTITUTIONAL PURCHASE ORDER, OR VALID CREDIT CARD NUMBER.

- ☐ 2000 VOLUME AT $40/$80
- ☐ 1999 VOLUME AT $40/$80
- ☐ 1998 VOLUME AT $40/$80
- ☐ 1997 VOLUME AT $40/$80
- ☐ 1996 VOLUME AT $40/$80
- ☐ 1995 VOLUME AT $35/$75
- ☐ 1994 VOLUME AT $35/$75
- ☐ 1993 VOLUME AT $30/$70
- ☐ 1992 VOLUME AT $30/$70
- ☐ 1990 VOLUME AT $30/$70

☐ CHECK ☐ PURCHASE ORDER ☐ VISA ☐ MASTERCARD

CARD OR PO# _____ EXP. DATE _____

SIGNATURE _____

AARC MEMBER # _____

NAME _____

INSTITUTION _____

ADDRESS _____

CITY _____ STATE _____ ZIP _____

NAME TO IMPRINT _____

DAEDALUS ENTERPRISES INC
PO BOX 29686 • DALLAS TX 75229 • FAX (972) 484-2720

Visit our online store at **http://www.aarc.org** where you can **order** all your respiratory **educational** & **promotional** items, including **books, audio cassettes, video-tapes, individual independent study packets,** and computer **software.**

Registered Respiratory Therapist

Up to $5,000 Sign-on Bonus!

Heartland Regional Medical Center, a progressive 246-bed Level II trauma center located in beautiful St. Joseph, MO, and recently rated as a **Top 100 Hospital** has immediate needs for high quality Registered Respiratory Therapists to help us continue our excellence in healthcare. We require an AS or BS from an accredited Respiratory Therapy program, and MO RCP Licence (or eligible). Full Time, Part Time and PRN openings for both day and night shifts are available now!

Come enjoy a career where you will be rewarded with a great new salary scale, sign-on bonus, moving expenses (if applicable), and/or additional compensation for education.

We offer superior career potential enhanced by family-friendly benefits which include Health/Dental/Vision after 30 days. Vacation, Sick & Holiday, Tuition Reimbursement for continued education, 401 (k) plan, Sick childcare and more. Apply online today at www.Heartland-Health.com, or call Jean Rush, (800) 443-1143, x 7502. Email: Jean.Rush@mail.Heartland-Health.com. EOE

Heartland Health

Circle 115 on product information card

The Buyer's Guide contains the latest information on companies and products as it is updated continually throughout the year. What's more, the Buyer's Guide is your source for information about new product releases. There are three main information resources: the Company Directory, the Equipment and Supplies Directory, and the Trademarks/Brand Names Directory. The product information you need is only a click away with our E-mail and URL links.

And, there's more to the Ultimate Online Buyer's Guide. One click at the Buyer's Guide gives you unbiased information to assist you in selecting the products you are considering for purchase. Access "Clinical Perspectives" articles from *AARC Times* and peer-reviewed articles from the science journal Respiratory Care. The Buyer's Guide is also one click away from the National Library of Medicine-Free Access to Medline.

VISIT THE BUYER'S GUIDE TODAY.

http://buyersguide.aarc.org/

Your Ultimate Resource for Locating Respiratory Product Information

The AARC Online BUYER'S GUIDE

The AARC Online Buyer's Guide is your ultimate resource for locating product information, company profiles and contacts, and trademarks and brand names.

Learn More About Mechanical Ventilation from the Experts

With Professional Education Products from the AARC.

Does the "Machine" Make a Difference?
Reviews different ventilators and modalities available to respiratory care practitioners and presents information on their impact in clinical settings. By John J. Marini, MD. 40-min. audiotape.
Item PAD86 $15.00 ($20.00 Nonmembers)

Unconventional Methods for Adult Oxygenation and Ventilation Support
Provides an overview of new and experimental techniques for adult oxygenation and ventilation support. Discusses the techniques, theoretical rationales, methods of application, and experimental evidence of the effectiveness of these unconventional methods. Featuring James K. Stoller, MD, and David J. Pierson, MD, FAARC. 90-min. videotape.
Item VC36 $49.95 ($99.00 Nonmembers)

Pressure-Controlled Ventilation (PCV): What's with the Pressure?
Reviews the status of PCV and compares the pressure and flow characteristics to those of volume ventilation. Discusses the advantages and disadvantages of PCV in specific patient populations. By Marshall L. Post, BHS, RRT. 40-min. audiotape.
Item PAD729 $15.00 ($20.00 Nonmembers)

Mechanical Ventilation: The Next 50 Years
Discusses the developments that are likely to occur over the next 50 years to address some of the issues of mechanical ventilation: more responsive valving systems with feedback loops, non-convective flow technology, pharmacologic adjustments, and more cost-efficient equipment. By Neil MacIntyre, MD, FAARC. 40-min. audiotape.
Item PAD752 $15.00 ($20.00 Nonmembers)

The Practice of Routine Ventilator Checks
Reviews the routine checking and documenting of mechanical ventilator functionality. Discusses the theoretical foundations for checking; details the regulatory and legal issues surrounding ventilator checks; and challenges some of the assumptions about routine ventilator checks. By John W. Salyer, RRT, FAARC. 40-min. audiotape.
Item PAD753 $15.00 ($20.00 Nonmembers)

Ventilator-Associated Pneumonia (VAP): Pathogenesis and Risk Factors
This lecture discusses hospital-acquired infection, specifically ventilator-associated pneumonia and its pathogenesis and risk factors. Demonstrates its occurrence as an independent determinant of mortality for critically ill patients requiring mechanical ventilation. By Marin H. Kollef, MD. 40-min. audiotape.
Item PAD789 $15.00 ($20.00 Nonmembers)

The Prevention of Ventilator-Associated Pneumonia (VAP) in the Year 2000
This lecture reviews new management strategies and the essential aspects of the pathogenesis of VAP, and the risk factors that predispose this infection. Clinical resources aimed at preventing the occurrence of VAP are also discussed. By Marin H. Kollef, MD. 40-min. audiotape.
Item PAD790 $15.00 ($20.00 Nonmembers)

Classification of Mechanical Ventilators I
Outlines the basic concepts of ventilator classification and a mathematical model of the respiratory system that provides the basis for classifying ventilator control systems. Also teaches the specific criteria for determining whether a ventilator primarily controls pressure, volume, or flow. Individual Independent Study Package. Softcover book.
Item CS18 $12.00 ($16.00 Nonmembers)

Classification of Mechanical Ventilators II
You will learn detailed information about the control of ventilation in terms of switching from inspiration to expiration. You will also be introduced to the common drive mechanisms used in various mechanical devices. Individual Independent Study Package. Softcover book.
Item CS19 $12.00 ($16.00 Nonmembers)

Classification of Mechanical Ventilators III
Explores the output waveforms that ventilators produce and their clinical implications. Instructs in the various modes of ventilation in terms of the specific combinations of control characteristics along with ventilator performance testing and the practical application of ventilator classification. Individual Independent Study Package. Softcover book.
Item CS20 $12.00 ($16.00 Nonmembers)

Measurement of Static Compliances and Dynamic Characteristics Curves During Mechanical Ventilation
Learn how to compute and record static compliance curves and dynamic characteristics. Also learn the procedure of obtaining pressure-volume measurements and interpret the compliance characteristics measurements. Individual Independent Study Package. Softcover book.
Item PE9 $12.00 ($16.00 Nonmembers)

Call (972) 406-4663 or Fax to (972) 484-2720 with MasterCard, Visa, or Purchase Order Number

---

Order Coupon

Charge to my ☐ Visa ☐ MasterCard Card expires _____

Card # _____

Signature _____

Payment enclosed $_____ Charge to Purchase Order #

_____

AARC Member # _____

Name/Institution _____

Address _____

_____

City/State/Zip _____

Valid AARC Member Number required for member prices. Prices are subject to change without notice. Texas Customers Only - Please add 8.25% sales tax. Texas exempt customers must attach exemption certificate.

Item #	Description	Quantity	Amount
		Item Subtotal	
		Shipping	
		Subtotal	
		Tx Sales Tax	
		Total	

Shipping and Handling Fees

Order Total	Ground	AK,HI,PR	International
$15 or less	$4.25	$12.25	$39.50*
$15.01 to $25	$5.25	$14.50	$44.00*
$25.01 to $40	$6.25	$17.00	$48.25*
$40.01 to $60	$7.25	$19.25	$52.50*
$60.01 to $80	$8.25	$21.50	$57.00*
$80.01 to $100	$9.25	$25.00	$65.50*
$100.01 to $150	$10.25	$30.75	$74.25*
$150.01 to $200	$12.25	$33.00	$78.50*
$200.01 to $250	$14.25	$39.00	$86.50*
$250.01 to $300	$16.25	$44.00	$95.75*
$300.01 and up	$18.25	$58.50	$114.25*
$400 or more	$20.25	$64.50	$119.25*

*International orders require an additional $15 for customs brokerage fee

Mail to: AARC, 11030 Ables Lane, Dallas, TX 75229-4593
(972) 243-2272 • FAX (972) 484-2720

Visit www.aarc.org for all your respiratory information needs.
For other products visit www.aarc.org/professional_resources/keys/

call for abstracts

RESPIRATORY CARE • OPEN FORUM 2002

48TH INTERNATIONAL RESPIRATORY CONGRESS • TAMPA, FLORIDA U.S.A.

The American Association for Respiratory Care and its science journal, RESPIRATORY CARE, invite submission of brief abstracts related to any aspect of cardiorespiratory care. The abstracts will be reviewed, and selected authors will be invited to present posters at the OPEN FORUM during the AARC International Respiratory Congress in Tampa, Florida, October 5-8, 2002. Accepted abstracts will be published in the August 2002 issue of RESPIRATORY CARE. Membership in the AARC is not required for participation. All accepted abstracts are automatically considered for ARCF research grants.

SPECIFICATIONS—READ CAREFULLY!

An abstract may report **(1) an original study, (2) the evaluation of a method, device or protocol, or (3) a case or case series.** Topics may be aspects of adult acute care, continuing care/rehabilitation, perinatology/pediatrics, cardiopulmonary technology, or health care delivery. The abstract may have been presented previously at a local or regional—but not national—meeting and should not have been published previously in a national journal. The abstract will be the only evidence by which the reviewers can decide whether the author should be invited to present a poster at the OPEN FORUM. Therefore, *the abstract must provide all important data, findings, and conclusions.* Give specific information. Do not write such general statements as "Results will be presented" or "Significance will be discussed."

ESSENTIAL CONTENT ELEMENTS

Original study. Abstract *must* include (1) Background: statement of research problem, question, or hypothesis; (2) Method: description of research design and conduct in sufficient detail to permit judgment of validity; (3) Results: statement of research findings with quantitative data and statistical analysis; (4) Conclusions: interpretation of the meaning of the results.

Method, device, or protocal valuation. Abstract *must* include (1) Background: identification of the method, device, or protocol and its intended function; (2) Method: description of the evaluation in sufficient detail to permit judgment of its objectivity and validity; (3) Results: findings of the evaluation; (4) Experience: summary of the author's practical experience or a lack of experience; (5) Conclusions: interpretation of the evaluation and experience. Cost comparisons should be included where possible and appropriate.

Case report. Abstract *must* report a case that is uncommon or of exceptional educational value and must include (1) Introduction: relevant basic information important to understanding the case, (2) Case Summary: patient data and response, details of interventions. (3) Discussion: content should reflect results of literature review. The author(s) should have been actively involved in the case and a case-managing physician must be a co-author or must approve the report.

submit your OPEN FORUM abstract electronically
visit www.rcjournal.com

FORMAT AND TYPING INSTRUCTIONS

Accepted abstracts will be photographed and reduced by 40%; therefore, the size of the original text should be *at least* 10 points. A font like Helvetica or Times makes the clearest reproduction. The first line of the abstract should be the title in all capital letters. Title should explain content. Follow title with names of all authors (including credentials), institution(s), and location; underline presenter's name. Type or electronically print the abstract *single spaced in one paragraph on a clean sheet of paper, using margins set so that the abstract will fit into a box no bigger than 18.8 cm (7.4") by 13.9 cm (5.5"), as shown on the reverse of this page.* Insert only one letter space between sentences. Text submission on diskette is allowed but must be accompanied by a hard copy. *Data may be submitted in table form, and simple figures may be included provided they fit within the space allotted. No figure, illustration, or table is to be attached to the abstract form.* Provide all author information requested. Standard abbreviations may be employed without explanation; new or infrequently used abbreviations should be spelled out on first use. Any recurring phrase or expression may be abbreviated, if it is first explained. Check the abstract for (1) errors in spelling, grammar, facts, and figures; (2) clarity of language; and (3) conformance to these specifications. An abstract not prepared as requested may not be reviewed. Questions about abstract preparation may be telephoned to Linda Barcus at (972) 406-4667.

ELECTRONIC SUBMISSION

We encourage electronic submission. Send all submissions to barcus@aarc.org. They will be acknowledged immediately via return e-mail. Mailed confirmation copies are not necessary, except that we ask you to fax a hard copy of your abstract so we can check it for accuracy against the electronic version. The fax number is 972-484-6010 (marked to the attention of Linda Barcus). **Paper size** should be 8.5" x 11" (approx 21 x 28 cm), with all 4 margins set to 1.5" (approx 4 cm). **Figures & Tables.** Save the text portion of your abstract in a Microsoft Word compatible file format. Excel is preferred for any accompanying graphics. If you do not have an Excel compatible format, save your graphics as TIFF or EPS files. Simply renaming a file with a .tif or .eps suffix will not work. Do not send Lotus files. Please send the figure as an attachment separate from the text. We can reduce it to the correct size, but unless you send the figure by itself, all we will have is an image that cannot be reproduced. The fax copy you send will show us the exact placement and size of the figure. Remember that all figures and tables will be greatly reduced in size, so keep them simple enough to be readable.

Deadline. The mandatory Deadline is April 30, 2002 (postmark). Authors will be notified of acceptance or rejection *by letter only*. These letters will be mailed by June 15, 2002.

Mailing Instructions. Mail (Do not fax!) 2 clear copies of the completed abstract form, diskette (if possible), and a stamped, self-addressed postcard (for notice of receipt) to:

2002 RESPIRATORY CARE OPEN FORUM
11030 Ables Lane
Dallas TX 75229-4593

RESPIRATORY CARE OPEN FORUM 2002 Abstract Form

18.8 cm or 7.4"

Set margin to 1.5" top, left, right, bottom.

Set paper size to 8 1/2" × 11"

13.9 cm or 5.5"

1. Title must be in all upper case (capital) letters, authors' full names and text in upper and lower case.
2. Follow title with all authors' names including credentials (underline presenter's name), institution, and location.
3. Do not justify (ie, leave a 'ragged' right margin).
4. **Do not use type size less than 10 points.**
5. All text and the table, or figure, must fit into the rectangle shown. (Use only 1 clear, concise table or figure.)
6. Submit 2 clean copies.

Mail original & 1 photocopy (along with postage-paid postcard) to

2002 RESPIRATORY CARE OPEN FORUM
11030 Ables Lane
Dallas TX 75229-4593

or e-mail it to
barcus@aarc.org

Deadline is April 30, 2002 (postmark)

Electronic Submission Is Now Available. Visit www.rcjournal.com to find out more

Presenter

Name & Credentials

Mailing Address

Voice Phone & Fax

Corresponding Author *If Different* from Presenter

Name & Credentials

Mailing Address

Voice Phone & Fax

Manuscript Preparation Guide

RESPIRATORY CARE welcomes original manuscripts related to the science and technology of respiratory care and prepared according to the following instructions and the *Uniform Requirements for Manuscripts Submitted to Biomedical Journals* (available at *http://www.icmje.org/index.html*). Manuscripts are blinded and reviewed by professionals with experience in the subject of the paper. Authors are responsible for obtaining written permission from the original copyright holder to use previously published figures and tables. Before publication, authors receive page proofs and are allowed to make only minor corrections. Accepted manuscripts are copy-edited for clarity, concision, and consistency with RESPIRATORY CARE's format. Published papers are copyrighted by Daedalus Inc and may not be published elsewhere without permission. Editorial consultation is available at any stage of planning or writing: contact the Editorial Office, 600 Ninth Avenue, Suite 702, Seattle WA 98104, (206) 223-0558, fax (206) 223-0563, E-mail: rejournal@aarc.org

Categories of Articles

Research Article: A report of an original investigation (a study). Must include: Title Page, Abstract, Key Words, Introduction, Methods, Results, Discussion, Conclusions, and References. May also include: Tables, Figures (if so, must include Figure Legends), Acknowledgments, and Appendixes.

Review: A comprehensive, critical review of the literature and state-of-the-art summary of a topic that has been the subject of at least 40 published research articles. Must include: Title Page, Outline, Abstract, Key Words, Introduction, Review of the Literature, Summary, and References. May also include: Tables, Figures (if so, must include Figure Legends), Acknowledgments, and Appendixes.

Overview: A critical review of a pertinent topic that has fewer than 40 published research articles. Same structure as Review Article.

Update: A report of subsequent developments in a topic that has been critically reviewed in RESPIRATORY CARE or elsewhere. Same structure as a Review Article.

Special Article: A pertinent paper not fitting one of the other categories. Consult with the Editor before writing or submitting such a paper.

Editorial: A paper addressing an issue in the practice or administration of respiratory care. It may present an opposing opinion, clarify a position, or bring a problem into focus.

Letter: A brief, signed communication responding to an item published in RESPIRATORY CARE or about other pertinent topics. Tables, Figures, and References may be included. The letter should be marked "For Publication."

Case Report: Report of an uncommon clinical case or a new or improved method of management or treatment. A case-managing physician must either be an author or furnish a letter approving the manuscript. Must include: Title Page, Abstract, Key Words, Introduction, Case Summary, Discussion, and References. May also include: Tables, Figures (if so, must include Figure Legends), and Acknowledgments.

Point-of-View: A paper expressing personal but substantiated opinions on a pertinent topic. Must include: Title Page, Text, and References. May also include: Tables and Figures (if so, must include Figure Legends).

Drug Capsule: A miniature review paper about a drug or class of drugs. Drug Capsules address pharmacology, pharmacokinetics, and/or pharmacotherapy.

Graphics Corner: A brief, instructive case report discussing and illustrating waveforms for monitoring or diagnosis. Must include: Questions, Answers, and Discussion.

PFT Corner: A brief, instructive case report arising from pulmonary function testing, accompanied by a review of the relevant physiology and appropriate references to the literature. Must include: Questions, Answers, and Discussion.

Test Your Radiologic Skill: A brief, instructive case report pertinent to respiratory care and involving imaging, including one or more radiographs or other images submitted as black and white glossy photographs that clearly illustrate the teaching points being made. Must include: Questions, Answers, and Discussion.

Preparing the Manuscript

Double-space the text and number the pages. Do *not* include author names, author institutional affiliations, or allusions to institutional affiliations anywhere except on the title page. On the Abstract page include the title but do not include author names. Begin each of the following on a new page: Title Page, Abstract, Text, Acknowledgments, References, each Table, each Figure, and each Appendix. Use standard English in the first person and active voice. Type all headings in initial-capital letters (eg, Introduction, Methods, Patients, Equipment, Statistical Analysis, Results, Discussion). Center the main section headings and place second-level headings on the left margin.

Abstract Please ensure that the abstract does not contain any facts or conclusions that do not also appear in the body text. Limit the abstract to no more than 250 words.

Key Words Include a list of 6 to 10 key words or key phrases in Research Articles, Reviews, Overviews, Special Articles, and Case Reports. Key words are best selected from the Medical Subject Headings (MeSH) used by MEDLINE and available at *http://www.nlm.nih.gov/mesh/meshhome.html*.

References. Assign reference numbers in the order that articles are cited in your manuscript. At the end of the manuscript, list the cited works in numerical order. Abbreviate journal names as in *Index Medicus*. List all authors. If the research has not yet been accepted for publication, cite the research as a personal communication (eg, Smith KR, personal communication, 2001); *however, you must obtain written permission from the author to cite his or her unpublished data.* Do not number such references; instead, make parenthetical reference in the body text of your manuscript. Example: "Recently, Jones et al found this treatment effective in 45 of 83 patients (Jones HI, personal communication, 2000)."

The following examples show RESPIRATORY CARE's style for references.

Paper accepted but not yet published:

Hess D. New therapies for asthma. Respir Care (year, in press).

Article in a journal carrying pagination throughout the volume:

Legere BM, Kavuru MS. Pulmonary function in obesity. Respir Care 2000;45(8):967-968.

Article in a publication that numbers each issue beginning with Page 1:

Kallstrom TJ. Focus on asthma—disease management: a role for the respiratory therapist. AARC Times 1999;23(Oct):16, 17, 19.

Corporate author journal article:

American Association for Respiratory Care. Clinical Practice Guideline. Removal of the endotracheal tube. Respir Care 1999;44(1):85-90.

Article in journal supplement: (Journals differ in numbering and identifying supplements. Supply information sufficient to allow retrieval.)

Barnes PJ. Endogenous inhibitory mechanisms in asthma. Am J Respir Crit Care Med 2000; 161(3 Pt 2):S176-S181.

Abstract in journal: (Abstracts citations are to be avoided, and those more than 3 years old should not be cited.)

Volsko TA, De Fiore J, Chatburn RL. Acapella vs flutter: performance comparison (abstract). Respir Care 2000;45(8):991.

Editorial in a journal:

Giordano SP. What's that sound? (editorial) Respir Care 2000;45(10):1167-1168.

Editorial with no author given:

The perils of paediatric research (editorial). Lancet 1999;353(9154):685.

Letter in journal:

Piper SD. Testing conditions for nebulizers (letter). Respir Care 2000;45(8):971.

Book: (For any book, specific pages should be cited whenever reference is made to specific statements or other content.)

Cairo JM, Pilbeam SP. Mosby's respiratory care equipment, 6th ed. St Louis: Mosby; 1999:76-85.

Corporate author book:

American Medical Association Department of Drugs. AMA drug evaluations, 3rd ed. Littleton CO: Publishing Sciences Group; 1977.

Chapter in book with editor(s):

Isono S. Upper airway muscle function during sleep. In: Loughlin GM, Carroll JL, Marcus CL, editors. Sleep and breathing in children: a developmental approach. (Lung Biology in Health and Disease, Vol 147, Claude Lenfant, Executive Editor.) New York/Basel: Marcel Dekker; 2000:261-291.

World Wide Web

American Lung Association. Trends in pneumonia, influenza, and acute respiratory conditions mortality and morbidity. February, 2000. http://www.lungusa.org/data. Accessed November 20, 2000.

Tables. Tables should be consecutively numbered. At the bottom of the table define and/or explain all abbreviations and symbols used in the table. For footnotes use the following symbols, superscripted, in the table body, in the following order: *, †, ‡, §, ‖, ¶, **, ††. If data include a "±" value, please indicate whether the value is a standard deviation or standard error of the mean.

Figures (illustrations). Figures include graphs, line drawings, photographs, and radiographs. All figures should be sharp black-and-white images and be camera-ready. Glossy prints are preferred, but a good laser print will do. Use only illustrations that clarify and augment the text. Radiographs should clearly illustrate the point being made and should be submitted as black-and-white glossy photographs. If color is essential to the figure, consult the Editorial Office for more information. In reports of animal experiments, use schematic drawings, not photographs. A letter of consent must accompany any photograph of an identifiable person. Number figures consecutively as Figure 1, Figure 2, etc. All the figures must be mentioned in the text. Every figure must have a legend (a title and/or description explaining the figure). Figure legends should appear as separate paragraphs at the end of the manuscript (after the References section), in the same computer file as the manuscript (not in a separate file, as with the tables and figures).

Do not create scanned versions of figures borrowed from other publications; clear photocopies are preferable. To include figures previously published in other publications you must obtain permission from the original copyright holder. Figures must be of professional quality and a copy of the article from which the figure came should be available.

Drugs. Precisely identify all drugs and chemicals used, giving generic (nonproprietary) names, doses, and methods of administration. Brand or trade names may be given in parentheses after generic names.

Commercial Products. In the text, parenthetically identify commercial products only on first mention, giving the manufacturer's name and location. Example: "We performed spirometry (1085 System, Medical Graphics, Minneapolis, Minnesota)." Provide model

numbers if available, and manufacturer's suggested price if the study has cost implications

Permissions: You must obtain written permission to use pictures of identifiable individuals or to name individuals in the Acknowledgments section. You must obtain written permission from the original copyright holder to use figures or tables from other publications. Copies of all applicable permissions must be on file at RESPIRATORY CARE before a manuscript goes to press. Copyright is most often held by the journal or book in which the figure or table originally appeared and applies to the creativity, style, and form in which the facts/data are presented to the reader; the facts themselves are not copyright-protectable. Therefore, permission is required to reproduce a table or figure directly, or with minor adaptations, from a journal or book, but permission is not required if data are extracted and presented in a new format. In that case, cite the source of the data as in the following example: "Adapted from Reference 23."

Ethics. When reporting experiments on human subjects, indicate that procedures were conducted in accordance with the ethical standards of the *World Medical Association Declaration of Helsinki* (see Respir Care 1997;42(6):635-636; also available at *http://www.wma.net/e/17-c_eparagraphnumbering.html*) or of the institution's committee on human experimentation. State that informed consent was obtained. Do not use patients' names, initials, or hospital numbers in text or illustrations. When reporting experiments on animals, indicate that the institution's policy, a national guideline, or a law on the care and use of laboratory animals was followed.

Statistics. Identify the statistical tests used in analyzing the data and give the prospectively determined level of significance in the Methods section. Report p values in the Results section. Cite only textbook and published article references to support choices of tests. Parenthetically identify any computer programs used. If data include a "±" value, please indicate whether the value is a standard deviation or standard error of the mean.

Units of Measurement. Express all measurements in SI (*Système International*) units (units and conversion factors listed at Respir Care 1997;42(6):640 and also available at *http://www.rcjournal.com/author_guide/*. Show gas pressures (including blood gas tensions) in millimeters of mercury (mm Hg).

Conflict of Interest. On the cover page, authors must disclose any liaison or financial arrangement they have with a manufacturer or distributor whose product is addressed in the manuscript or with the manufacturer or distributor of a competing product. Such arrangements do not disqualify a paper from consideration and are not disclosed to reviewers. Reviewers are screened for possible conflict of interest.

Abbreviations and Symbols. Use the standard abbreviations and symbols listed at Respir Care 1997;42(6):637-642 (also available at *http://www.rcjournal.com/author_guide/*). Do not create new abbreviations. Do not use abbreviations in the title or section headings and do not use unusual abbreviations in the abstract. Use an abbreviation only if the term occurs 4 or more times in the paper. Parenthetically define *all* abbreviations: write out the full term on first mention, followed by the abbreviation in parentheses. Example: chronic obstructive pulmonary disease (COPD). Thereafter use only the abbreviation. Standard units of measurement and scientific terms can be abbreviated without explanation (eg, L/min, mm Hg, pH, O_2).

Please use the following forms: cm H_2O (not cmH2O), f (not bpm), L (not l), L/min (not LPM, l/min, or lpm), mL (not ml), mm Hg (not mmHg), pH (not Ph or PH), $p > 0.001$ (not p>0.001), s (not sec), S_{pO_2} (arterial oxygen saturation measured via pulse-oximetry).

Prior and Duplicate Publication In general, do not submit work that has been published or accepted elsewhere, though in special instances the Editor may consider such material if the original publisher grants permission. Please consult the Editor before submitting such work.

Authorship. All persons listed as authors must have participated in the reported work and in the shaping of the manuscript, all must have proofread the submitted manuscript, and all should be able to publicly discuss and defend the paper's content. A paper of corporate authorship must specify the key persons responsible for the article. Attribution of authorship is not based solely on solicitation of funding, collection or analysis of data, provision of advice, or similar services. Persons who provide such ancillary services may be recognized in an Acknowledgments section, but written permission is required from the persons acknowledged.

Reviewers: Please supply the names, credentials, affiliations, addresses, and phone/fax numbers of 3 professionals whom you consider expert on the topic of your paper. Your manuscript may be sent to one or more of them for blind peer review.

Submitting the Manuscript

Submit 3 printed copies and one (3.5-inch) computer diskette. The printed copies should each include photocopies of all of the Figures, Tables, and Appendixes. On the diskette, the manuscript should be in one file and the tables in a separate file. If soft copies of the figures are available, they should also be in a separate file. *However, do not create scanned versions of figures borrowed from other publications; clear photocopies are preferable.* Include the completed Cover Letter and Checklist (see next page) and permission letters. Mail to RESPIRATORY CARE, 600 Ninth Avenue, Suite 702, Seattle WA 98104. Do not fax manuscripts. Receipt will be acknowledged.

RESPIRATORY CARE
Editorial Office:

600 Ninth Avenue, Suite 702
Seattle WA 98104

(206) 223-0558 (voice)
(206) 223-0563 (fax)
rcjournal@aarc.org

Cover Letter & Checklist

A copy of this completed form must accompany all manuscripts submitted for publication.

Title of Paper: _____

Publication Category: _____

Corresponding Author: _____ Phone: _____ FAX: _____

Mailing Address: _____

Reprints: ❑ Yes ❑ No E-mail Address: _____

"We, the undersigned, have all participated in the work reported, proofread the accompanying manuscript, and approve its submission for publication." Please print and include credentials, title, institution, academic appointments, city and state. If more than 4 authors, please use another copy of this form.*

*First Author: _____

Author Signature/Date _____

*Second Author: _____

Author Signature/Date _____

*Third Author: _____

Author Signature/Date _____

*Fourth Author: _____

Author Signature/Date _____

Has this research been presented in any public forum? ❑ Yes ❑ No

If yes, where, when and by whom? _____

Has this research received any awards? ❑ Yes ❑ No

If yes, please describe. _____

Has this research received any grants or other support, financial or material? ❑ Yes ❑ No

If yes, please describe. _____

Do any of the authors of this manuscript have a financial interest in (or a commercial or consulting relationship to) any of the products or manufacturers mentioned in this paper or any competing products or manufacturers? ❑ Yes ❑ No

If yes, please describe. _____

CHECKLIST

- ❑ Have you enclosed a copy of the manuscript on diskette?
- ❑ Is double-spacing used throughout entire manuscript?
- ❑ Are all pages numbered in upper-right corners?
- ❑ Are all references, figures, and tables cited in the text?
- ❑ Has the accuracy of the references been checked, and are they correctly formatted?
- ❑ Have SI values been provided?
- ❑ Has all arithmetic been checked?
- ❑ Have generic names of drugs been provided?
- ❑ Have necessary written permissions been provided?
- ❑ Have authors' names been omitted from text and figure labels?
- ❑ Have copies of 'in press' references been provided?
- ❑ Has the manuscript been proofread by all the authors?
- ❑ Have the manufacturers and their locations been provided for all devices and equipment used?

American Association for Respiratory Care **Membership Application**

ACTIVE MEMBER
An individual is eligible if he she lives in the U S or its territories or was an Active Member prior to moving outside its borders or territories and meets ONE of the following criteria (1) is legally credentialed as a respiratory care professional if employed in a state that mandates such OR (2) is a graduate of an accredited educational program in respiratory care, OR (3) holds a credential issued by the NBRC

ASSOCIATE OR SPECIAL MEMBER
Individuals who hold a position related to respiratory care but do not meet the requirements of Active Member shall be Associate Members. They have all the rights and benefits of the Association except to hold office vote or serve as chair of a standing committee The following subclasses of Associate Membership are available Foreign, Physician, and Industrial (individuals whose primary occupation is directly or indirectly devoted to the manufacture sale or distribution of respiratory care equipment or supplies) Special Members are those not working in a respiratory care-related field

STUDENT MEMBER
Individuals will be classified as Student Members if they meet all the requirements for Associate Membership and are enrolled in an educational program in respiratory care accredited by, or in the process of seeking accreditation from, an AARC-recognized agency

SPECIAL NOTICE — Student Members do not receive Continuing Respiratory Care Education (CRCE) transcripts Upon completion of your respiratory care education, continuing education credits may be pursued upon your reclassification to Active or Associate Member

Please read the eligibility requirements for each of the classifications above, then complete the form. All information requested must be provided, except where indicated as optional. See other side for more information and fee schedule. Please sign and date application on reverse side and type or print clearly. Processing of application takes approximately 15 days.

- Active
- Associate
  - Foreign
  - Physician
  - Industrial
- Special
- Student

Last Name _____

First Name _____

Social Security No. _____

Home Address _____

City _____

State _____ Zip __ __ __ __ __ - __ __ __ __

Phone No. (_____) _____

Work Information:

PLEASE USE THE ADDRESS OF THE LOCATION WHERE YOU PERFORM YOUR JOB, NOT THE CORPORATE HEADQUARTERS IF IT IS LOCATED ELSEWHERE

Place of Employment _____

Address _____

City _____

State _____ Zip __ __ __ __ __ - __ __ __ __

Phone No. (_____) _____

Preferred Fax No. (_____) _____

Preferred Email Address _____

Preferred mailing address: Home Business

Would you like to receive our monthly newsletter, AARC Report, by email?

Yes No

Have you ever been or are you currently in the military?

Yes No

Demographic Questions (optional)

We request that you answer these questions in order to help us design services and programs to meet your needs.

Primary Job Responsibility (check one only)

- Director (Technical or Program)
- Supervisor
- Diagnostic Technologist
- Instructor/Educator
- Other, specify _____
- Therapist/Technician
- Medical Director
- Student
- Staff Nurse

Type of Business

- Educational Institution
- DME/HME
- Home Health Agency
- Hospital/Acute Care
- Other, specify _____
- Manufacturer or supplier
- Outpatient Clinic
- Physician office
- Skilled Nursing Facility

Check the Highest Degree Earned

- High School
- RC Graduate Technician
- Associate Degree
- Bachelor's Degree
- Master's Degree
- Doctorate Degree

Number of Years in Respiratory Care

- 0-2 years
- 3-5 years
- 6-10 years
- 11-15 Years
- 16 years or more

Job Status

- Full Time
- Part Time

Credentials

- RRT
- CRT
- Physician
- CRNA
- RN
- LVN/LPN
- CPFT
- RPFT
- Perinatal/Pediatric

Date of Birth _____ Sex _____

FOR STUDENT MEMBER – REQUIRED

School/RC Program _____

Address _____

City _____

State _____ Zip __ __ __ __ __ - __ __ __ __

Phone No. (_____) _____

Expected Date of Graduation (REQUIRED INFORMATION)

Month _____ Year _____

American Association for Respiratory Care • 11030 Ables Lane • Dallas, TX 75229-4593 • (972) 243-2272 • Fax (972) 484-2720

American Association for Respiratory Care Membership Application

Membership Fees

Payment must accompany your application to the AARC. Fees are for 12 months. These fees contain the $12.50 new members processing fee. Renewing members (except students) can deduct $12.50.

CHOOSE ONE LEVEL OF MEMBERSHIP

1. AARC REGULAR MEMBERSHIP (Receive both AARC Times and Respiratory Care journal)

☐ Active	$87.50
☐ Associate (Industrial or Physician)	$87.50
☐ Associate (Foreign)	$102.50
☐ Special	$87.50
☐ Student	$45.00

OR

2. AARC CHOICE MEMBERSHIP(Choose one publication)

☐ Active	$76.00
☐ Associate (Industrial or Physician)	$76.00
☐ Associate (Foreign)	$91.00
☐ Special	$76.00

I want ☐ AARC Times ☐ Respiratory Care journal

OR

3. AARC PLUS MEMBERSHIP (All publications and other items)

☐ Active	$122.50
☐ Associate (Industrial or Physician)	$122.50
☐ Associate (Foreign)	$162.50
☐ Special	$122.50

Specialty Sections (optional)

Established to recognize the specialty areas of respiratory care, these sections publish a newsletter four times a year that focuses on issues of specific concern to that specialty. The sections also design the specialty programming at the national AARC meetings.

☐ Adult Acute Care Section	$15.00
☐ Education Section	$20.00
☐ Perinatal-Pediatric Section	$15.00
☐ Diagnostics Section	$15.00
☐ Continuing Care-Rehabilitation Section	$15.00
☐ Management Section	$20.00
☐ Transport Section	$15.00
☐ Home Care Section	$15.00
☐ Subacute Care Section	$15.00

PLEASE SIGN

I hereby apply for membership in the American Association for Respiratory Care and have enclosed my dues. If approved for membership in the AARC, I will abide by its bylaws and professional code of ethics. I authorize investigation of all statements contained herein and understand that misrepresentations or omissions of facts called for is cause for rejection or expulsion

A yearly subscription to RESPIRATORY CARE journal and *AARC Times* magazine includes an allocation of $11.50 from my dues for each of these publications

NOTE Contributions or gifts to the AARC are not tax deductible as charitable contributions for income tax purposes However, they may be tax deductible as ordinary and necessary business expenses subject to restrictions imposed as a result of association lobbying activities The AARC estimates that the nondeductible portion of your dues — the portion which is allocable to lobbying — is 26%

Signature _____

Date _____

TOTAL MEMBERSHIP FEE $_____

TOTAL SECTION FEE $_____

GRAND TOTAL = Membership Fee plus optianal sections

$_____

☐ Total Amount Enclosed $_____

☐ Please charge my dues (see below)

To charge your dues, complete the following:

☐ MasterCard

☐ Visa

Card Number

_ _ _ _ _ _ _ _ _ _ _ _ _ _ _ _

Card Expires _____/_____

Signature _____

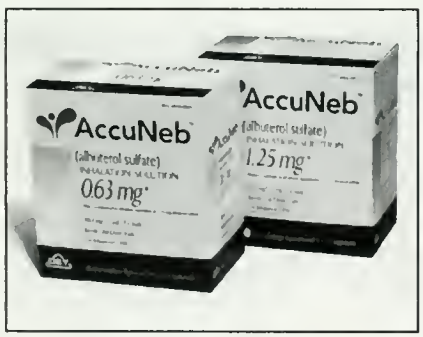
Mail application and appropriate fees to:

American Association for Respiratory Care • 11030 Ables Lane • Dallas, TX 75229-4593 • (972) 243-2272 • Fax (972) 484-2720

News releases about new products and services will be considered for publication in this section. There is no charge for these listings. Send descriptive release and glossy black and white photographs to RESPIRATORY CARE, New Products & Services Dept, 11030 Ables Lane, Dallas TX 75229-4593. The Reader Service Card can be found at the back of the Journal.

New Products & Services

Cloth Adhesive Tape. 3M™ Cloth Adhesive Tape used for securing medical devices and immobiliation support now comes latex free with higher initial adhesion, according to the manufacturer. 3M claims that the new and improved hypoallergenic tape is formulated to adhere well to dry or damp skin and will leave less residue on the patient's skin. They further say that the cloth adhesive tape is economical and easy to use, tearing easily both crosswise and lengthwise. For more information from 3M, circle number 187 on the reader service card in this issue, or send your request electronically via "Advertisers Online" at http://www.aarc.org/buyers_guide/



Albuterol Sulfate Inhalation Solution for Pediatrics. Dey, LP, has announced FDA approval of AccuNeb (albuterol sulfate) inhalation solution for patients two to 12 years of age with asthma. According to the manufacturer, AccuNeb provides the first pediatric-specific albuterol preparation to the US market; it contains no benzalkonium chloride and is available in sterile and preservative-free unit-dose vials. Dey states that AccuNeb complies with the National Asthma Education and Prevention guidelines for pediatric asthma patients, and is available in two concentrations: 1.25 mg and 0.63 mg (potency expressed as albuterol, equivalent to 1.5 mg and 0.75 mg albuterol sulfate). For more information from Dey, circle number 188 on the reader service card in this issue, or send your request electronically via "Advertisers Online" at http://www.aarc.org/buyers_guide/

Evaluating Protective Devices Guide. ECRI has announced the availability of *Sharps Safety and Needlestick Prevention*, a comprehensive new guide for evaluating and selecting protective devices. This new resource updates and expands on the 2000 edition of ECRI's *Health Devices Needlestick-Prevention Device Selection Guide*. According to ECRI, *Sharps Safety and Needlestick Prevention* features comparative evaluations, including brand-name ratings, for more than 60 currently available "safety" devices in 13 different product groups, including never-before published evaluations of 34 new devices. For more information from ECRI, circle number 189 on the reader service card in this issue, or send your request electronically via "Advertisers Online" at http://www.aarc.org/buyers_guide/

Electronic Oxygen Conserver. Chad Therapeutics Inc announces the introduction of its new SEQUOIA OXYMATIC electronic oxygen conserver, available in two models: the SEQUOIA 302 AND 311. The SEQUOIA conservers offer the same electronic technology found in the OXYMATIC 400 Series conservers, but without a built-in regulator, according to the manufacturer. The manufacturer also says that the model 302 and 311 conservers provide the same choice between alternate breath and every breath technology, along with other features of the 400 Series—including expanded flow rates to 6 L/m, increased shot sizes to service a wider segment of the home oxygen patient population, utilize standard supply tubing and cannula connections, and provide superior oxygen conservation with an average 5:1 savings over continuous flow. For more information from Chad Therapeutics, circle number 190 on the reader service card in this issue, or send your request electronically via "Advertisers Online" at http://www.aarc.org/buyers_guide/

Sleep Apnea Therapy Device. Weinmann of Hamburg has introduced *Somnocomfort*, a new nCPAP sleep apnea therapy device. According to the manufacturer, the new device features an outstanding noise suppression system and absolutely sure pressure constancy for the settings determined in the sleep lab. *Somnocomfort* is equipped with an autostart activated by the patient's light breathing, an integrated therapy calendar, a double filter system (fine and coarse), and an actual pressure display, says Weinmann. If required, claims the manufacturer, the newly developed heated humidifier *Somnoclick* can be attached to the front of the device without extra hoses or power cables. For more information from Weinmann, circle number 191 on the reader service card in this issue, or send your request electronically via "Advertisers Online" at http://www.aarc.org/buyers_guide/

Notices

Notices of competitions, scholarships, fellowships, examination dates, new educational programs, and the like will be listed here free of charge. Items for the Notices section must reach the Journal 60 days before the desired month of publication (January 1 for the March issue, February 1 for the April issue, etc). Include all pertinent information and mail notices to RESPIRATORY CARE Notices Dept, 11030 Ables Lane, Dallas TX 75229-4593

Scheduled Professor's Rounds 2002

Withholding and Withdrawing Life Support in the ICU — Gordon D Rubenfeld MD / Richard D Branson BA RRT FAARC — Live February 12; Audio March 5

Weaning from Mechanical Ventilation: New Insights, New Guidelines — Neil R MacIntyre MD FAARC/ Dean R Hess PhD RRT FAARC — Live April 16; Audio May 14

Neonatal and Pediatric Ventilators: What's the Difference? — Mark J Heulitt MD FAAP FCCP/ Richard D Branson BA RRT FAARC — Live May 21; Audio June 25

Ventilator Graphs: What's with That Wave? — Jon O Nilsestuen PhD RRT FAARC/ Richard D Branson BA RRT FAARC —Live July 16; Audio August 13

Talking with Patients and Families About Death and Dying— Helen M Sorensen MA RRT/ David J Pierson MD FAARC —Live August 20; Audio September 17

Pressure vs: Volume Ventilation: Does It Matter? — Robert S Campbell RRT FAARC/ Richard D Branson BA RRT FAARC — Live September 10/ Audio October 8

Inpatient Management of COPD — Randall Rosenblatt MD/ David J Pierson MD FAARC — Live October 22; Audio November 12

High-Frequency Oscillatory Ventilation — Thomas E Stewart MD/ Richard D Branson BA RRT FAARC — Live November 19; Audio December 10

Helpful Web Sites

American Association for Respiratory Care
http://www.aarc.org
- — Current job listings
- — American Respiratory Care Foundation fellowships, grants, & awards
- — Clinical Practice Guidelines

National Board for Respiratory Care
http://www.nbrc.org

RESPIRATORY CARE online
http://www.rcjournal.com
- — Subject and Author Indexes
- — Contact the editorial staff
- — OPEN FORUM; submit your abstract online

Asthma Management Model System
http://www.nhlbi.nih.gov

Keys to Professional Excellence
http://www.aarc.org/keys/

Committee on Accreditation for Respiratory Care
http://www.coarc.com

The National Board for Respiratory Care— Examination Fees for 2001

Examination	Examination Fees
CRT	$190 (new applicant) $150 (reapplicant)
Perinatal/Pediatric	$250 (new applicant) $220 (reapplicant)
CPFT	$200 (new applicant) $170 (reapplicant)
RPFT	$250 (new applicant) $220 (reapplicant)
RRT (Written & CSE)	$190 (new) $150 (reapplicant) written only $200 (new and reapplicant) CSE only $390 (new) $350 (reapplicant) both

For information about other services or fees, write to the National Board for Respiratory Care, 8310 Nieman Road, Lenexa KS 66214, or call (913) 599-4200, FAX (913) 541-0156, or e-mail: nbrc-info@nbrc.org

Not-for-profit organizations are offered a free advertisement of up to eight lines to appear, on a space available basis, in Calendar of Events in RESPIRATORY CARE. Ads for other meetings are priced at $5.50 per line and require an insertion order. Deadline is the 20th of the month two months preceding the month in which you wish the ad to run. Submit copy and insertion orders to Calendar of Events, RESPIRATORY CARE, 11030 Ables Lane, Dallas TX 75229-4593

Calendar of Events

Date	AARC & State Society Programs	Contact
Dec. 1–4	47th International Respiratory Congress; **San Antonio, TX**	AARC, (972) 243-2272, www.aarc.org
Feb. 6–8, 2002	West Virginia Society for Respiratory Care's Winter Meeting; **Davis, WV**	Jay Wildt at (304) 442-7474 or jay.wildt@mghwv.org; or Anna Parkman at (304) 357-4837 or AParkman@ucwv.edu.
Feb. 6–8, 2002	Oregon Society's Pacific Northwest RC Conference; **Portland, OR**	Tim Mixdorf at (503) 537-1570 or tmixdorf@providence.org

Date	Other Meetings	Contact
Nov. – Feb.	Deep South Center for Occupational Health and Safety offers an assortment of RC continuing education courses lasting from one to four days; **Birmingham, AL**	Melinda Sledge, University of Alabama at Birmingham, (205) 934-7178, www.uab.edu/dsc
March 12–13, 2002	Practical Spirometry Course; **Rochester, MN**	Mayo Pulmonary Services,Mayo Clinic, (800) 533-1653
March 20–23, 2002	21st Annual Big Sky Pulmonary & Critical Care Medicine Conference; **Big Sky, MT**	American Lung Association of the Northern Rockies, (406) 442-6556, ala-nr@ala-nr.org

Coming in 2002

Two Special Issues on Invasive Mechanical Ventilation in Adults: Implementation, Management, Weaning, & Follow-Up

29th RESPIRATORY CARE Journal Conference Papers and Discussions

Conference Co-Chairs: Richard D Branson RRT FAARC Charles G Durbin Jr MD FAARC

Authors in This Issue

Barry, Henry C 1450
Bazzell, C Mark 1454
Camargo, Carlos A 1380
Cook, Deborah J 1408
Durbin Jr, Charles G 1392
Edmonds, Marcia L 1380
Flemons, W Ward 1418
Guyatt, Gordon H 1408
Heitman, Steven J 1418
Herridge, Margaret S 1368
Littlewood, Keith 1392
Meade, Maureen O 1368, 1408
Nelson, Steven B 1455, 1456
Rowe, Brian H 1380
Rubenfeld, Gordon D 1442
Slonim, Anthony D 1451
Spooner, Carol H 1380
Thomas, Patricia A 1452
Tonelli, Mark R 1435, 1453

Advertisers in This Issue

To advertise in RESPIRATORY CARE, contact Tim Goldsbury, Director, Advertising Sales, e-mail: goldsbury@aarc.org for rates and media information. Contact Karen Camlet, Advertising Representative, e-mail: camlet@aarc.org, for recruitment/classified advertising. Sales office: 380 Tequesta Drive, Tequesta, FL 33469, Telephone: (561) 745-6793, Fax: (561) 745-6795.

Send production materials for AARC publications to Binkley @aarc.org or AARC 11030 Ables Lane, Dallas TX 75229-4593 c/o Beth Binkley

Circle #	Company	Page #	Phone	Fax	E-mail/Website
120	ABW	1351	(888) 460-8733		abw@fbcc.com
128	Clear Medical	1338	(800) 426-1042		www.clearmedical.com
129	Compumedics	C3	(877) 717-3975	(763) 717-3973	www.compumedicsusa.com
119	Dey	C2, 1329, 1330	(800) 755-5560		www.deyinc.com
102	DHD Healthcare	C4	(800) 847-8000		www.dhd.com
130	Ferraris Medical Inc	1361	(800) 205-7187		www.ferrarismedicalusa.com
159	Hans Rudolph	1359	(800) 456-6695		www.rudolphkc.com
115	Heartland Health	1483	(800) 443-1143		Jean.Rush@mail.Heartland-Health.com
110	Hy-Tape	1363	(800) 248-0101	(845) 878-4104	www.hytape.com
114	Masimo	1332	(877) 4-MASIMO		www.masimo.com
117	Monaghan Medical	1341	(800) 833-9653		www.monaghanmed.com
116	Monaghan Medical	1345	(800) 833-9653		www.monaghanmed.com
108	Nellcor/Puritan Bennett	1353			
111	Praxair	1334	(800) 299-7977		www.praxair.com/healthcare
109	Puritan Bennett/Tyco Healthcare	1339	(800) 635-5267		
112	ResMed	1336	(800) 424-0739		www.resmed.com
103	Respironics Healthscan	1343	(800) 962-1266		www.respironics.com
106	Salter Labs	1347	(800) 235-4203		www.salterlabs.com
105	Spectrum Health	1482	(619) 238-3609	(619) 238-3551	jhornaday@spectrumhealth.com
113	Tech Net Medical, LLC	1357	(800) 461-1815	(888) 782-3358	www.technetmedical.com
104	Texas Health Resources	1355	(866) JOBS THR	(866) 889-8978	www.TexasHealth.org
118	Vortran Medical	1349	(916) 948-8460	(916) 648-9751	www.vortran.com

COPYRIGHT INFORMATION. RESPIRATORY CARE is copyrighted by Daedalus Enterprises Inc. Reproduction in whole or in part without the express written permission of Daedalus Enterprises Inc is prohibited. Permission to photocopy a single article in this Journal for noncommercial purposes of scientific or educational advancement is granted. Permission for multiple photocopies and copies for commercial purposes must be requested in writing, via e-mail (rejournal@aarc.org), or telephone and approved by RESPIRATORY CARE. Anyone may, without permission, quote up to 500 words of material in this journal provided the quotation is for noncommercial use and RESPIRATORY CARE is credited. Longer quotation requires written approval by the author and publisher. Single reprints are available only from the authors. Reprints for commercial use may be purchased from Daedalus Enterprises Inc. For more information and prices call (972) 243-2272.

DISCLAIMER. The opinions expressed in any article or editorial are those of the author and do not necessarily reflect the views of the Editors, the American Association for Respiratory Care (AARC), or Daedalus Enterprises Inc. Neither are the Editors, the AARC, or the Publisher responsible for the consequences of the clinical applications or use of any methods or devices described in any article or advertisement.

SUBSCRIPTION RATES. Individual subscription rates are $75 per year (12 issues), $145 for 2 years, and $215 for 3 years in the US and Puerto Rico. Rates are $90 per year, $175 for 2 years, and $260 for 3 years in all other countries (add $94 per year for air mail). Single copies when available cost $10; add $9 for air mail postage to overseas countries. Checks should be made payable to RESPIRATORY CARE and sent to the subscription office at 11030 Ables Lane, Dallas TX 75229-4593, or call (972) 243-2272.

SUBSCRIPTION RATES FOR ASSOCIATIONS. Basic annual subscriptions are offered to members of associations according to their membership enrollment: 101-500 members = $16.25/year (each); 501-1,500 = $15.75/year (each); 1,500-10,000 = $14.75/year (each); more than 10,000 = $13.75/year (each). For information, contact Ray Masterrer at (972) 243-2272.

CHANGE OF ADDRESS. Notify the AARC at (972) 243-2272 as soon as possible of any change in address. Note the subscription number (from the mailing label) and your name, old address, and new address. Allow 6 weeks for the change. To avoid charges for replacement copies of missed issues, requests must be made within 60 days in the US and 90 days in other countries.

MANUSCRIPTS. The Journal publishes clinical studies, method/device evaluations, reviews, and other materials related to cardiopulmonary medicine and research. Manuscripts may be submitted to the Editorial Office, RESPIRATORY CARE, 600 Ninth Avenue, Suite 702, Seattle WA 98104. Instructions for authors are printed in every issue.

Subscription

Respiratory Care Subscription Form

Respiratory Care is the most highly regarded peer-reviewed scientific publication for the Clinician participating in the evaluation and care of patients with cardiopulmonary problems. Please print; incomplete forms will not be processed. For faster service, fax to (972)484-2720

DON'T MISS A SINGLE ISSUE!

	U.S. Subscriptions	Subscriptions Outside U.S.
1 YR (12 Issues)	☐ $75	☐ $90
2 YRS (24 Issues)	☐ $145	☐ $175
3 YRS (36 Issues)	☐ $215	☐ $260

Enclosed is a check in the amount of $ _____

Charge to my:
- ☐ Mastercard
- ☐ Visa
- ☐ Bill Me

Signature _____ Expiration Date _____ Credit Card Number _____

Name _____ Title _____

Facility Name _____

Address _____

City _____ State _____ Zip Code _____ Country _____

Telephone _____ Fax _____

RESPIRATORY CARE

FREE

Product Information

Receive FREE information on the products and services mentioned in this issue, by circling the corresponding advertiser's number. Fill in your name and address and mail this postage-paid card. Information will be sent directly to you from the manufacturer. Incomplete forms will not be processed.

MAIL TODAY
OR FOR FASTER SERVICE
FAX TO
(609) 786-4115

For AARC membership information, circle 101. For Respiratory Care subscription information, circle 102.

101	102	103	104	105	106	107	108	109	110	111	112	113	114	115	116	117	118
119	120	121	122	123	124	125	126	127	128	129	130	131	132	133	134	135	136
137	138	139	140	141	142	143	144	145	146	147	148	149	150	151	152	153	154
155	156	157	158	159	160	161	162	163	164	165	166	167	168	169	170	171	172
173	174	175	176	177	178	179	180	181	182	183	184	185	186	187	188	189	190
191	192	193	194	195	196	197	198	199	200								

Please circle no more than 15 items.

Name _____ Title _____

Facility Name _____

Address _____

City _____ State _____ Zip Code _____ Country _____

Telephone _____ Fax _____

December 2001 Expires 3/15/02

RESPIRATORY CARE

I TYPE OF INSTITUTION OR PRACTICE
1 ☐ Hospital
2 ☐ Skilled Nursing Facility
3 ☐ Subacute Care Facility
4 ☐ Home Care Practice
5 ☐ School
6 ☐ Distributor

II DEPARTMENT
A ☐ Respiratory Care
B ☐ Cardiopulmonary
C ☐ Subacute Care
D ☐ Home Care

III SPECIALTY
1 ☐ Clinician
2 ☐ Perinatal/ Pediatrics
3 ☐ Critical Care
4 ☐ Research
5 ☐ Subacute Care
6 ☐ Diagnostics/ Pulmonary Function
7 ☐ Management
8 ☐ Home Care
9 ☐ Rehabilitation
10 ☐ Education

IV POSITION
A ☐ Department Head
B ☐ Chief Therapist
C ☐ Supervisor
D ☐ Staff Therapist/ Technician
E ☐ Medical Director
F ☐ Educator/Instructor
G ☐ Sales
H ☐ Other (please specify) _____

V ARE YOU AN AARC MEMBER?
1 ☐ Yes 2 ☐ No

fier

nt.
:e.

ern
ory.

COMPUMEDICS LIMITED

Authors in This Issue

Barry, Henry C 1450
Bazzell, C Mark 1454
Camargo, Carlos A 1380
Cook, Deborah J 1408
Durbin Jr, Charles G 1392
Edmonds, Marcia L 1380
Flemons, W Ward 1418
Guyatt, Gordon H 1408
Heitman, Steven J 1418
Herridge, Margaret S 1368
Littlewood, Keith 1392
Meade, Maureen O 1368, 1408
Nelson, Steven B 1455, 1456
Rowe, Brian H 1380
Rubenfeld, Gordon D 1442
Slonim, Anthony D 1451
Spooner, Carol H 1380
Thomas, Patricia A 1452
Tonelli, Mark R 1435, 1453

Adverti in This Is

Circle #	Compan
120	ABW
128	Clear Me
129	Compum
119	Dey
102	DHD He:
130	Ferraris M
159	Hans Ru
115	Heartlan
110	Hy-Tape
114	Masimo
117	Monagha
116	Monagha
108	Nellcor/H
111	Praxair
109	Puritan B
112	ResMed
103	Respiron
106	Salter La
105	Spectrun
113	Tech Net
104	Texas He
118	Vortran M

COPYRIGHT INFORM
Daedalus Enterprises Inc written permission of D photocopy a single artic scientific or educationa photocopies and copies ing, via e-mail (rejourna RATORY CARE. Anyon material in this journal p RESPIRATORY CARE proval by the author and authors. Reprints for cor terprises Inc. For more i

DISCLAIMER. The opi of the author and do n American Association prises Inc. Neither are t for the consequences of vices described in any a

SUBSCRIPTION RATI (12 issues), $145 for 2 Rico. Rates are $90 per y

NO POSTAGE NECESSARY IF MAILED IN THE UNITED STATES

BUSINESS REPLY MAIL

FIRST-CLASS MAIL PERMIT NO. 2480 Dallas,TX

POSTAGE WILL BE PAID BY ADDRESSEE

AARC Subscriptions

ATTN: Beth Binkley
PO BOX 29686
Dallas TX 75229-9691

NO POSTAGE NECESSARY IF MAILED IN THE UNITED STATES

BUSINESS REPLY MAIL

FIRST-CLASS MAIL PERMIT NO. 881 Riverton, NJ

POSTAGE WILL BE PAID BY ADDRESSEE

AARC Publications

PO BOX 11605
Riverton NJ 08076-7205

e Series™ PSG Advanced, Network-Linked Amplifier

In life, being well connected can be quite important. In a sleep lab, it makes all the difference.

Compumedics' new e-Series amplifier captures the power of modern computer networking and brings it directly to your sleep laboratory.

e-Series Integrated Networking Functions

- Simple set up with standard CAT 5 network cable
- Control or view any e-Series from any computer on the network
- Stream waveforms and video in real-time
- Access e-Series units across wide area networks
- Record directly to any computer on the LAN or WAN
- Record from up to 4 e-Series amplifiers on a single computer (2 per computer with digital video)

Powerful e-Series Clinical Advantages

- 44 amplified channels
- 57 Total available signals
- Up to 512Hz sampling, channel selectable
- Integrated Oximeter and 2 Pressure Transducers
- Record any montage without compromises
- Sophisticated digital video option
- Use the same amplifier for full 32 channel EEG with optional ProFUSION EEG software

Your System is Your Network.
We can show you why.

COMPUMEDICS LIMITED

For more information please contact

Compumedics Australia: 1 Marine Pde, Abbotsford, VIC, 3067, Australia, Phone: +613 9419 5433, Fax: +613 9419 5488, Web: www.compumedics.com.au
Compumedics USA, Inc: 7950 University Avenue NE, Fridley, Minnesota 55432, Phone: 1 763 717 3975, Fax: 1 763 717 3973, Toll Free USA: 877 717 3975, Web: www.compumedicsusa.com

B0199_2

Circle 129 on product info card

New acapella.® Vibratory PEP therapy from a whole new perspective.

It works in virtually any position, with virtually any patient.

Vibratory PEP Therapy

- Improves clearance of secretions.
- Easier to tolerate than CPT.
- Less than half the time of conventional CPT session*.
- Facilitates opening of airways in patients with lung diseases with secretory problems (COPD, asthma, Cystic Fibrosis).

Tired of confining patients to an uncomfortable, upright position for vibratory PEP? With new acapella, you don't have to take that sitting down! Its unique design permits use while standing, reclining or walking. So now everyone from active pediatrics, to bedridden patients, can benefit from secretion clearance therapy. Color-coded units (green for high-flow, blue for low) help you customize treatment based on clinical needs. You can adjust acapella's frequency and flow resistance simply by turning an adjustment dial. And because therapy can be self-administered in any setting, you'll provide an effective continuum of care outside the hospital. For the new generation of vibratory PEP therapy, call DHD Healthcare toll-free today: **1-800-847-8000. acapella.** ***No instrumental accompaniment required.***

* Mahlmeister MJ et al. "Positive-expiratory pressure mask therapy. Theoretical and Practical Considerations and a Review of the Literature." *Respiratory Care*. 1994.

DHD Healthcare

Innovations for respiratory care

One Madison Street, Wampsville, NY 13163 USA
(800) 847-8000 · (315) 363-2330 · FAX (315) 363-5694
www.dhd.com

acapella is a registered trademark of DHD Healthcare Corporation
© 2001 DHD Healthcare Corporation

MEDICAL DESIGN EXCELLENCE AWARDS™ 2001 WINNER

Circle 102 on product information card